Patentability of New Claims 41 and 42.

Without acquiescing to the above grounds for rejection, Applicants present new claims 41 and 42. These claims set forth the subject matter of determining if the patient is infected with CMV. None of the references cited by the Examiner in the instant rejections disclose or suggest the diagnosis of CMV infection prior to administration of any neuroleptic of the recited formula.

In so far as the cited references fail to disclose all the elements of claims 41 and 42, Applicants note that the above grounds for rejection are an insufficient basis for rejecting claims 41 and 42 and respectfully that they be allowed.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

Frank J. Mycroft
Reg. No. 46,946

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Attachments
FJM:kar
60217134 v1

PATENT
Attorney Docket No.: 019934-000310US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 9088
Thomas J. Schall, et al.	Examiner: Jiang, S. Anna
Application No.: 09/944,163	Technology Center/Art Unit: 1617
Filed: August 30, 2001	
For: MODULATORS OF US 28	Declaration of Edward S. Mocarski, Jr., under 37 C.F.R. § 1.132
Customer No.: 20350	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Professor Edward S. Mocarski, Jr., being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 U.S.C. § 1001), and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true, and statements made on information or belief are believed to be true and correct.

2. I received my Ph.D. in Microbiology from the University of Iowa, Iowa City, Iowa. I received my A.B. in Microbiology from Rutgers University, New Brunswick, New Jersey. I was a United States Public Health Service postdoctoral trainee in Virology and a Leukemic Society of America Special Fellow at the University of Chicago, Chicago, Illinois. I am presently a Professor in the Department of Microbiology and Immunology at Stanford University School of Medicine, Stanford, California. From 1995-1999, I served as Chairman of the Department, and, from 2000-2001, I served as the Associate Dean of Research of Stanford University. I serve and have served on the editorial board for a number of Journals in the field of virology. I serve or have served on a number of national review panels concerning infectious

disease, including CMV, and immunology. I am the author of well over one hundred scientific papers in the field of microbiology, many of which primarily address CMV. A true copy of my *Curriculum Vitae* is attached hereto as Exhibit A.

3. Research in my laboratory primarily focuses on one of the human herpesviruses: cytomegalovirus (CMV). This virus is a major medical problem in immunocompromised individuals. The virus is very large, and carries over 200 genes. We have characterized functions involved in viral growth (regulation of gene expression, replication, genome packaging) and pathogenesis (tissue tropism, latency). Importantly, molecular genetic and biochemical approaches have been employed to dissect these functions. Many current efforts have been made possible by our development of genetic methodology to engineer precise mutations into the viral genome. Viral functions regulating tissue tropism and latency are currently a major focus of ongoing work. We have found that CMV resides latent in bone marrow hematopoietic cells and have characterized viral gene functions during latency. My areas of current interest include:

- Genetic and biochemical analysis of functions involved in regulation of viral gene expression, including transcriptional regulatory proteins as well as functions that regulate posttranscriptional events.
- Analysis of the DNA replication origins employed by CMV to replicate the viral genome during lytic and latent growth, and to identify viral functions involved in replication and alteration of the host cell.
- Signals and mechanisms involved in replication and packaging of herpesvirus genomes.
- Genetic and biochemical analysis of functions involved in latency and reactivation.

4. I am and have been a consultant to ChemoCentryx on technical matters.

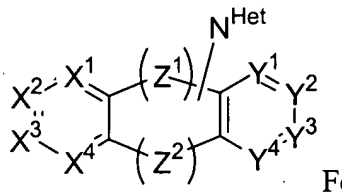
5. I am not a named inventor on the above-referenced patent application. I have read and am familiar with the contents of the specification. I have also read the portions of the Office Actions mailed July 29, 2003; January 14, 2004; and March 31, 2004 which allege the claimed subject matter to be obvious. I have also reviewed the references relied upon the Examiner to support the allegations.

From such, it is my understanding that the Examiner is concerned that the subject matter of the claims may not conform to the nonobviousness provisions of 35 U.S.C. §103(a)

over Protiva et al. (U.S. Patent No. 4,243,805) in view of the Merck Manual of Diagnosis and Therapy (17th Ed.) and Michelson (Eur. Cytokine Netw. 10(2): 286-287 (1999)). It is also my understanding that the Examiner is additionally concerned that the subject matter of the claims may not conform to the nonobviousness provisions of 35 U.S.C. §103(a) over Sindelar et al. in view of the Merck Manual of Diagnosis and Therapy (17th Ed.) and Michelson (Eur. Cytokine Netw. 10(2): 286-287 (1999)).

The inventive subject matter of the claims is based upon the discovery that the compounds of Formula I specifically inhibit the binding of fractalkine to the CMV US28 receptor and that compounds which bind to the US28 receptor can be useful in the treatment of CMV infection and slowing the progression of CMV dissemination in a host.

For the reasons set forth herein, it is my belief that at the time of the invention, one of skill in the art would **not** have predicted that the compounds of the general formula



Formula I

as further defined in amended base claims 5 and 29 set forth in the Amendment mailed March 15, 2004 could be used to inhibit CMV infection itself or to slow the progression or the dissemination of CMV in the infected human host.

Prior to the filing of the earliest priority applications (i.e., August 30, 2000), I believe one of ordinary skill in the art would not have known and could not have predicted that the compounds of Formula I were specific ligands of the CMV US28 chemokine receptor. Rather, one or ordinary skill in the art would recognize such compounds as stereospecific ligands of catecholamine receptors, particularly, dopamine and serotonin receptors. One of ordinary skill in the art would have known that the US28 receptor specifically bound chemokines such as fractalkine. Such chemokines are very different molecules than the comparatively much smaller and structurally different natural ligands for dopamine or serotonin receptors or the organic compounds of the above formula. By way of distinction, fractalkine is a protein of about 76 amino acids in length and has a molecular weight of about 8-9 kdaltons. At the time of filing, I believe one of ordinary skill in that art would regard the biological activities, roles, and binding properties of the US28 *viral* receptor and the CNS *mammalian* receptors mediating the CNS effects of neuroleptics to be distinctly different. The ability to of the US28 receptor to specifically bind such chemokines would thus simply not have lead one of ordinary skill in the art to expect that the US28 receptor could specifically bind any compounds of the above formula.

As a corollary, I believe one of ordinary skill would not have expected administration of any neuroleptic compound to occupy the US28 receptor so as to affect CMV dissemination or to be useful in treating CMV infection by affecting CMV dissemination.

As of August 30, 2000, I believe one of ordinary skill in the art would recognize, as taught by Protiva *et al.*, that the compounds of the above formula encompass useful neuroleptic and psychotropic agents. However, I also believe that one of ordinary skill in the art would recognize as taught in the above-referenced Merck Manual that CMV infection can cause CNS damage and injury, typically during congenital exposure during pregnancy, but not principally in neonates, children or adults, even when immunocompromised and susceptible to CMV-induced disease. I also believe that one of ordinary skill in the art would recognize that CMV *congenital* infection can cause mental retardation and that CMV can replicate in a variety of cell types. However, serious CNS injury only occurs in 1-5% of CMV congenital infections. One of ordinary skill in the art would also appreciate that whether a neuroleptic agent of the above formula would be useful, harmful or of no effect at all in treating such CNS damage and injury would be a highly individualized matter and depend greatly upon the extent(s) and particular site(s) of the injury. I also believe one of ordinary skill in the art would understand that the neuroleptic therapy envisoned in the Office Action(s) to operate via receptors involved in neurotransmission (e.g., dopaminergic, serotoninergic receptors) would not operate via the viral US28 receptor. More particularly, in any such instances, one of ordinary skill in the art would appreciate that the administration was done in order to modulate neurotransmission in the CNS and not for the purpose of modulating CMV dissemination in the happenstance of an active or persistent CMV infection. Indeed, even in those hypothetical instances where use of a neuroleptic of Formula I might be useful in the treatment of the CNS sequelae of a CMV infection by modulation of neurotransmission, such a benefit would exist even in the absence of any on-going active infection with the CMV virus. Thus, at best, any inherency which could arise in the Examiner's posited scenario would be at most a mere possibility and would certainly not be a consistent, necessary, or inevitable aspect of the proposed combination.

In conclusion, it is respectfully submitted that prior to the discoveries set forth in the specification, one of skill in the art would **not** have had a reasonable basis to expect that compounds of Formula I could be used to treat CMV infection or to prevent CMV dissemination in a host as set forth in the instant claims. It is also respectfully submitted that prior to those discoveries, one of skill would **not** have known or predicted that neuroleptic drugs could be useful, rather than harmful, in treating infectious diseases let alone CMV. It is further submitted

that prior to this invention, one of skill in the art would **not** have predicted that the compounds of Formula I could specifically bind to the US 28 receptor.

The declarant has nothing further to say.

Professor Edward S. Mocarski, Jr.

May 11, 2004
Date

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	Telephone: (650) 854-9114

Education and Employment Record:

Rutgers University, New Brunswick, New Jersey	A.B. Microbiology	1970-74
University of Iowa, Iowa City, Iowa	Ph.D. Microbiology	1974-79
USPHS Predoctoral Trainee in Cellular and Molecular Biology		1975-78
The University of Chicago, Chicago, Illinois	Postdoctoral	1979-83
USPHS Postdoctoral Trainee in Virology		1979-81
Leukemia Society of America Special Fellow		1981-83
Stanford University School of Medicine, Stanford, California		
Assistant Professor of Microbiology & Immunology		1983-89
Associate Professor of Microbiology & Immunology		1989-95
Chairman of the Department of Microbiology & Immunology		1995-99
Professor of Microbiology & Immunology		1995-pres
Stanford University, Stanford, California		
Associate Dean of Research		2000-01

Sabbatical leave:	SyStemix, Palo Alto, California	1990 (6 mo.)
	Aviron, Mountain View, California	1995 (6 mo.)

National Review Panel Memberships (current membership in Bold):

NIH Reviewers Reserve/ad hoc reviews (1994-2007)
NIDOCD Review Panel on CMV-related Hearing Loss (2004)
Advisory Panel to Office of AIDS Res on Opportunistic Infections (1995-96)
NIH-NIAID Spec Review: Molec. & Struc. Appr. Antiviral Drug Design (1994)
NIH Experimental Virology Study Section (1990-1994)
NIH-NIAID Special Review - Animal Models of Human Viral Infections (1990)
NIH-NIAID Workshop on Opportunistic Infections in AIDS (1989)
NIH Small Business Administration Study Section (1988)
USDA Biotechnology Study Section (1986-88)

Ad Hoc Panel Member: NIH Clinical Sciences I Study Section (1985), NIH Site Visit Panels (1986, 1987), NIH Virology Study Section (1988), NIH-NIAID Microbiology and Infectious Disease Research Committee (1989), USDA-Hatch Grant Program Reviewer - University of Nevada (1989), NIH-NIAID Board of Scientific Counselors (1989), USDA Biotechnology Study Section (1989-95), Natural Sciences and Engineering Research Council of Canada (1992).

Court-appointed expert: US 9th District Court (Federal Judge advisor) (1998-03)

Editorial Board (current membership in Bold):
Journal of Virology **(1991-2006),** ***Virology*** **(1991-2004),** ***J. Biol. Chem*** **(2001-2004)** *Journal Biol. Chem* (1994-1999), *Intervirology* (1986-1989)

Invited Reviewer:
Journals: *Science, Journal of General Virology, Virus Research, Intervirology, Archives of Virology, Proceedings of the National Academy of Sciences, Journal of Clinical Microbiology, Journal of Infectious Diseases, New England Journal of Medicine, Journal of Experimental Medicine, Blood, Journal of Immunology, Immunity, Cell*

Grants: National Science Foundation, Veterans Administration, National Foundation March of Dimes, Wellcome Foundation, United Kingdom MRC, Canadian Blood Service, Canadian MRC, USDA

Honors and Awards:

Pfizer Visiting Professor in Infectious Diseases, Univ of Oklahoma (2001)
Elkin's Lecture, Emory University (1999)
ASM Foundation for Microbiology Lecturer (1992-94)
National Institutes of Health Wallace Rowe Lecture (1993)
American Cancer Society Faculty Research Grant (1984-1993)
Leukemia Society of America Special Fellow (1981-1983)
Agnes Axtell Moule Faculty Scholar (1983)
Andrew Mellon Fellow (1984)

Professional Affiliations:

American Society for Microbiology
American Society for Virology

Stanford Committees (current membership listed in bold):
Chair, School of Medicine Conflict of Interest Committee (2001-2004).
Senator at Large, School of Medicine Senate
Alternate Chair, Administrative Panel of Biosafety (2002-2004).
Member, Stanford University on Committee Land and Building Development (2003-2006)

Past member: Stanford University Committee on Research (2000), Research Council for the Medical School (1997-1999) ex officio 2000, Cellular Basis of Disease Training Program Committee (1994-1999), Faculty Performance Evaluation Committee (1997-1998), Space Utilization Task Force (1996-1998), Academic Council Committee on Graduate Studies (1995-1998) Chair: 1996-1998, Administrative Panel on Laboratory Animal Care (1992-1995), Chair, Review Committee for Program in Immunology (1992), Medical School Faculty Senate Alternate (1988-1992), Administrative Panel of Biosafety (1983-1989), Cancer Biology Program Committee (1987-1990), Subcommittee on Medical School Endowment (1987), Task Force on Admissions Procedures (1986-1988), Committee on Courses and Curriculum (1988-1990), Medical Scholars Committee (1989-1990), Medical Scientist Training Prog. Comm. (1984-1995; 2000-2004) Assist. Director, 1984-1994.

Teaching: Department of Microbiology and Immunology:
MI206 - Animal Viruses, Course Director (1984-present)
MI210 - Pathogenesis of Viral, Bacterial and Eukaryotic Pathogens (1998-present)
MI212 - Advanced Immunology (2001 - present)
MI220A - Host:Parasite Interaction and Host Defense for Medical Students (1998)
MI208 - Topics in Virology, 10 lecture hours (1987, 1994, 1997, 2001)
MI202 - Medical Microbiology, coordinator of virology lecturers (1983-90); Course Co-Director (1991), lecturer (1992-1999)
MM101 - General Microbiology, 3 lecture hours (1986-1988, 1994)
MM103 - Medical Virology for undergrads, 6 lecture hours (1989-90)
MM207 - Pathogenesis of Infect. Diseases, 1 lecture hour (1986-89)
Ethics - The Responsible Conduct of Research, 2 lecture hours (2001-02)

Other Departments/Institutions:
CBio 243 - Cancer Biology, 4 lecture hours (1988-2001)
UC Berkeley - Virology, 1 lecture hour (1992-2000)

Consultant :

Current Program Projects:

Nebraska Center for Virology (COBRA), P.I. Wood (2000 - present)
Herpes Oncogenesis, Latency & Reactivation, P.I. Raab-Traub (1995-pres)

Current Companies:

ChemoCentryx (1997-2007)
GlobeImmune (2003-2008)

Past or Occasional:

9th District Court, Judicial Scientific Advisor (2000-2003); ImmunoGen, Inc. (1995-2002); GeneTrol (2001-2002); MedImmune, Inc. (1992-2002) (called Aviron from 1992-2002); Ribozyme Pharmaceuticals, Inc. (1992-2001); Parke-Davis (Warner-Lambert) (1998-1999); Glaxo-Wellcome Herpesvirus Consultancy Group (1996-1998); Searle-Monsanto, Skokie, Illinois (1994-1995); Chiron Corporation, Emeryville, California (1991-92); Schering-Plough, Inc., Madison, New Jersey (1984-1994); Syntro, Inc., San Diego, California (1985-88); SyStemix, Palo Alto, California (1990)

Active Grant Awards (Direct costs only):

NIH RO1 AI20211-20 Cytomegalovirus DNA Replication and Inversion.
PI: Ed Mocarski (Stanford SPO #573)
Period: 3/01/84 - 11/31/07; $200,000 current year
15% effort

NIH RO1 AI30363-10 Cytomegalovirus Pathogenesis in Immunodeficiency
PI: Ed Mocarski (Stanford SPO #8045)
Period 4/01/91 - 6/30/06 $175,000 current year.
15% effort

NIH RO1 AI33852-10 Cytomegalovirus Gene Regulation in Immunodeficiency
PI: Ed Mocarski (Stanford SPO #11160)
Period: 8/01/94 - 6/30/04; $160,465 current year.
15% effort

NIH PO1 CA49605 - 16 Program Project: Bone Marrow Grafting for Leukemia and Lymphoma. PI: Rob Negrin (Stanford SPO #6095)
Project IX: Latency and Reactivation of Cytomegalovirus after Bone marrow Transplantation. Project leader: Mocarski
Period: 2/01/97 - 1/31/07; $128,581 current year
5% effort

NIH PO1 AI50153-03 (Mocarski, PI) Program Project in Immunopathogenesis of Chronic Graft Rejection. Title: Transplant Arteriosclerosis (TA): Viral and Host Mechanisms" (Stanford SPO #24386)
Project 2 Cytomegalovirus Control of Cell Proliferation and Inflammation (Mocarski, PL)
Period 09/10/01 - 06/31/06 $922,030 overall/yr ($158,910 to ESM/Project 2) 18% effort

Pending (Requested direct costs):

NIH PO1 HL79355 (Mocarski PI) Program Project "Transplant Arteriopathy (TA): Viral and Host Mechanisms" Project 2 Cytomegalovirus Control of Cell Proliferation and Inflammation (Mocarski, PL)
Requested first year direct costs: $1,336,291 ($189,053 to Project 2)

Present Laboratory Members: *(Year joined or period in laboratory)*

Predoctoral	Postdoctoral
Geoffrey Smith (2000)	Laura Hertel, Ph.D., University of Turin (1999)
	Satoshi Noda, Ph.D., University of Kanazawa (2002)
	Christopher Meiering, Ph.D., Univ. of Washington (2002)
	Hamish Smith, Ph.D, Washington University (2003)
	David AuCoin, Ph.D, University of Nevada, Reno (2003)

Past Sabbatical: Marie Jo Masse, Ph.D. (1991-92)
Lawrence Corey, M.D. (1994)
Dana Wolfe, M.D. (1998-99)
Maria Paola Landini (1999)

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University of Western Australia (1994)
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Shinya Watanabe, M.D. Ph.D. (1996-99)
Associate Professor

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Barry Slobedman, Ph.D. (1995-99)
Lecturer

Millenium Institute
University of Sydney
Westmead Hospital
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Sydney State 2145 AUSTRALIA

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Fredrick S. Leach, M.D. Ph.D. (1984-90; M.D. Ph.D., 1990)
Assistant Professor

Urology and Molecular and Human Genetics
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Baylor College of Medicine
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Dora Y. Ho, M.D. Ph.D. (1984-90; Ph.D., 1990; M.D., 2001)
(currently in postgraduate clinical training)

Dept of Internal Medicine
Santa Clara Valley Medical Center
751 South Bascom Avenue
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doraywho@hotmail.com

Charmain Tan Courcelle, Ph.D. (1993-00, Ph.D. 2000)
(currently Postdoctoral fellow)

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Major Invited and Plenary Presentations:

1984 Keystone/UCLA Symposium - Herpesvirus
1985 International Herpesvirus Workshop - Ann Arbor
1986 International Herpesvirus Workshop - Leeds
1987 Animal Cells and Viruses Gordon Conference - Tilton
International Congress of Virology - Edmonton
1988 Transfusion-Associated Infections and Immune Response - San Francisco
Banbury Conference on Virus Vectors - Cold Spring Harbor
The Albany Conference - Viral Vectors - Troy
International Herpesvirus Workshop - Irvine
1989 First US-Japan Biotechnology Meeting - St. Petersburg
Second International Cytomegalovirus Workshop - San Diego
1990 Pathogenesis of Cytomegalovirus-Associated Diseases - Irvine
Annual Meeting of German Virologists - Ulm
International Congress of Virology - Berlin
International Herpesvirus Workshop - Georgetown
1991 3rd International Cytomegalovirus Workshop - Bologna
5th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections - St Petersberg
1992 IRBM Meeting on The Molecular Basis of Viral Latency - Rome
NIH Child Health and Human Development Workshop on Congenital CMV - Bethesda
First International Herpesvirus Symposium in Japan - Osaka
Banbury Conference on Molecular Mechanisms of Viral Latent Infections - Cold Spring Harbor
1993 Wallace Rowe Symposium - NIH, Bethesda
UCLA Symposium: Molecular Biology of Human Pathogenic Viruses - Lake Tahoe
4th International Cytomegalovirus Conference - Paris
6th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections - Hokkaido
1994 International Society for Antiviral Research - Charleston
Collaborative Antiviral Program - NIH, Bethesda
American Society for Microbiology Annual Meeting - Las Vegas
19th International Herpesvirus Workshop - Vancouver
4th International Meeting of the Canadian Bone Marrow Transplantation - Ottawa
1995 5th International Cytomegalovirus Workshop - Stockholm
20th International Herpesvirus Workshop - Groningen, Netherlands
7th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections - St. Petersberg, FL
1996 Glasgow Virology Workshop, Scotland

Consensus Symposium on Advances in Diagnosis, Treatment and Prophylaxis of CMV Infection - Sanibel Island, FL
21st International Herpesvirus Workshop - DeKalb, IL

1997 136th Society for General Microbiology General Meeting - Reading, United Kingdom
Animal Viruses Gordon Conference - Tilton, NH
8th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections - Mishima, Japan
Ocular Herpesvirus Research Workshop, Granlibakken, CA
37th Interscience Conference on Antimicrobial Agents and Chemotherapy - Toronto, Canada

1998 National Advisory Allergy and Infectious Diseases Council - Pathogen Genome Sequencing and Beyond, Bethesda, MD.

1999 Elkin Lecture, Emory University.
CMV Retinitis - 2nd Multidisciplinary Research Workshop, Yosemite, CA
7th International Cytomegalovirus Workshop, Keynote, Bristol, England
Robert H. Lurie Cancer Center Basic Science Colloquium, Chicago, IL
9th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections - Lucca, Italy
Danish Royal Biology Society lecture, Copenhagen

2000 Consensus Conference: Prevention of Post-Transfusion CMV in the Era of Universal Leukoreduction, Toronto
FASEB Microbial Pathogenesis Summer Conference, Aspen
3rd Symposium on Cytomegalovirus-related Immunopathology, Bertinoro, Italy
CDC Cytomegalovirus Vaccine Workshop, Altanta
University of Oklahoma Pfizer Visiting Professor in Infectious Diseases

2001 Keystone Conference: Control of Viral Latency and Persistence
Keystone Conference:Molecular Aspects of Viral Immunity
8th International Cytomegalovirus Workshop, Pacific Grove
Gordon Conference on Viruses and Cells, Lucca, Italy
26th International Herpesvirus Workshop, Regensburg, Germany
39th Infectious Disease Society of America Meeting, San Francisco
Inauguration Symposium - Virology Institute of Tubingen University
NIH NIAID Viral Mechanism of Immune Evasion Workshop, Annapolis
10th International Conference on Immunobiology and Prophylaxis of Herpesvirus Infections, Osaka.

2002 American Transplant Congress, Washington, DC
Foundation Juan March Viral Immunomodulation, Madrid
Trudeau Institute, Saranac Lake
International Joint Meeting on Cytokines (Cytokines 2002), Turin

2003 9th International Cytomegalovirus Workshop/1st International Betaherpesvirus Workshop, Maastricht

7th Symposium on Virus-Host Interactions, Mt Sinai School of Medicine
2004 Keystone Symposium, The Pathogen:Host Standoff - Taos

Other Invited Seminars and Presentations:

1985 UC Los Angeles, Syntro, UC Irvine, DNAX Research Institute, Animal Cells and Viruses Gordon Conference, American Society of Virology
1986 University of Nevada, Dupont Research, Schering Research
1987 Chiron Corp., University of Chicago, University of Alabama, University of Kentucky, Scripps Clinic and Research Foundation, DNAX, UC San Francisco
1988 University of Rochester, Schering Research, Syntex Corp., University of Washington, University of Minnesota, Louisiana State University, NIH National Cooperative Vaccine Discovery Groups in AIDS Workshop, Gilead Sciences
1989 University of Chicago, Miles Laboratories, Schering Research
1990 University of British Columbia - Vancouver, SyStemix Corp., US Biochemical Corp., University of North Carolina, Research Triangle Virology Group, University of Ulm, University of Bologna, University of Washington, Genentech
1991 University of Missouri Medical Center-Columbia, University of Tennessee -Knoxville, Protein Design Labs, University of Turin, Schering Research, Irwin Memorial Blood Center, University of Ferrara, SmithKline Beechem Corp., BioMega, Jefferson Medical College
1992 UpJohn Corp., Louisiana State University, Linus Pauling Institute, ICLAM Forum Lake Tahoe, International Herpesvirus Workshop - Edinburgh, University of Western Australia - Perth, University of Melbourne, Institute for Medical and Veterinary Sciences - Adelaide, Ribozyme Pharmaceuticals Corp.
1993 Michigan State University, Palo Alto Medical Foundation, 18th International Herpesvirus Workshop - Pittsburgh, UC San Francisco, University of Osaka, Royal Free Medical School - London, UC Davis, University of Washington
1994 University of Pennsylvania Medical School, Aviron Corp - Burlinghame, 19th International Herpesvirus Workshop - Vancouver, City of Hope Medical Center - Duarte, University of California - Irvine, Gilead Sciences - Foster City
1995 Northwestern University Medical School, McMaster University School of Medicine, University of Southern California School of Medicine, Harvard University School of Medicine, University of Colorado - Boulder, University of Gothenberg, Cambridge University, Smithkline Beechem Pharmaceuticals - Epson, Animal Viruses Gordon Conference - Tilton, 20th International Herpesvirus Workshop - Goningen, Scripps Research Institute, Smithkline Beechem Pharmaceuticals - King of Prussia.

1996 University of Glasgow, University of Bologna, Smithkline Beechem Biologicals - Belgium, St. Jude Children Research Hospital, University of Kansas, SmithKline Beechem Pharmaceuticals - King of Prussia.

1997 University of Nebraska, CMV Retinitis (A Multidisciplinary Workshop)-San Francisco, University of Tennessee-Knoxville, University of Pennsylvania, Oregon State University of the Health Sciences, UCSF Center for AIDS Research, University of British Columbia-Vancouver, University of Rijeka-Croatia, Robarts Research Institute-London, Ontario.

1998 St. Jude Children Research Hospital, Children's National Research Hospital, Ribozyme Pharmaceutical, Inc., Cytomegalovirus Latency Discussion Group, Keystone Symposium on Molecular Aspects of Viral Immunity, 23rd International Herpesvirus Workshop, UC Berkeley Program in Microbial Biology, University of Michigan, Parke-Davis Pharmaceuticals, Gladstone Institute for Virology, University of North Carolina.

1999 State University of New York at Buffalo, Northwestern University, University of Turin, University of Bologna, Baylor College of Medicine, University of Illinois School of Medicine-Chicago, Fox Chase Cancer Center, University of Munich

2000 University of Massachusetts

2001 University of California, Los Angeles; University of Iowa; Cleveland Clinic and Research Institute; University of Nebraska; University of North Carolina; University of Edmonton; UCSF-Gladstone Research Foundation; International Congress of Immunosuppression, San Diego; Northwestern University School of Medicine, Chicago.

2002 Vaccine Research Center of NIAID-NIH, Bethesda; ImmunoGen, Cambridge; Fred Hutchinson Cancer Research Center, Seattle; Ohio State University, Columbus; Ohio University, Athens; University of Sydney School of Medicine; ViroPharma, Exton; University of Padua, Italy.

2003 University of Maastricht, Netherlands; Imperial College School of Medicine, London; University of California, San Diego; University of Mainz, Germany; University of Pavia, Italy, Washington University, St. Louis; University of California – Irvine.

2004 Duke University Medical School, Louisiana State University Medical School – Shreveport.

Meetings Organized:

Major Meetings:

1991 XVI International Herpesvirus Workshop - Asilomar (850 participants)
2001 8th International Cytomegalovirus Workshop - Asilomar (350 participants)
2004 Keystone Symposium, The Pathogen:Host Standoff - Taos

Workshops:

1987 West Coast Herpesvirus Workshop - Asilomar (95 participants)
1989 West Coast Herpesvirus Workshop - Asilomar (120 participants)
1990 West Coast Herpesvirus Workshop - Asilomar (130 participants)
1992 West Coast Herpesvirus Workshop - Asilomar (80 participants)
1993 West Coast Herpesvirus Workshop - Asilomar (85 participants)
1995 West Coast Herpesvirus Workshop - Reno (70 participants)
1998 Cytomegalovirus Latency Discussion Group - Tucson (18 participants)

International Organizing Committee:

1992 XVII International Herpesvirus Workshop - Edinborough
1993 XVIII International Herpesvirus Workshop - Pittsburg
1993 4th International Cytomegalovirus Conference - Paris
1994 XIX International Herpesvirus Workshop - Vancouver
1995 5th International Cytomegalovirus Conference - Stockholm
1995 XX International Herpesvirus Workshop - Groningen
1997 6th International Cytomegalovirus Conference - Alabama
1997 XXII International Herpesvirus Workshop - San Diego
2001 XXVI International Herpesvirus Workshop – Regensburg
2004 XXIX International Herpesvirus Workshop – Reno

PUBLICATIONS

Journals:

1. **Mocarski, E.S. and M.F. Stinski** (1979). Persistent infection of human fibroblast cells by human cytomegalovirus. **J. Virol.** 31:761-775.

2. **Stinski, M.F., E.S. Mocarski, D.R. Thomsen and M. Urbanowski** (1979). Membrane glycoproteins and antigens induced by cytomegalovirus. **J. Gen. Virol.** 43:119-129.

3. **Stinski, M.F., E.S. Mocarski and D.R. Thomsen** (1979). Some properties of cytomegalovirus DNA from standard and defective virions. **J. Virol.** 31:231-239.

4. **Post, L.E., A.J. Conley, E.S. Mocarski and B. Roizman** (1980). Cloning of reiterated and nonreiterated herpes simplex 1 sequences as BamHI fragments. **Proc. Natl. Acad. Sci. USA** 77:4201-4205.

5. **Mocarski, E.S., L.E. Post and B. Roizman** (1980). Molecular engineering of herpes simplex virus genome: Insertion of a second L-S junction into the genome causes additional genome inversions. **Cell** 22:243-255.

6. Mocarski, E.S. and B. Roizman (1981). The site specific inversion sequence of the herpes simplex virus genome: Domain and structural features. **Proc. Natl. Acad. Sci. USA** 78:7047-7051.

7. **Mocarski, E.S. and B. Roizman** (1982). Herpesvirus dependent amplification and inversion of cell-associated viral thymidine kinase gene flanked by viral *a* sequences and linked to an origin of viral DNA replication. **Proc. Natl. Acad. Sci. USA** 79:5626- 5630.

8. **Mocarski, E.S. and B. Roizman** (1982). The structure and function of the herpes simplex virus DNA termini: Implications regarding circularization, inversion and generation of virion DNA. **Cell** 31:89-97.

9. **Spaete, R.R. and E.S. Mocarski** (1984). Trans-acting functions encoded by herpes simplex virus-1 recognize cis cleavage/packaging signals present on cytomegalovirus DNA. In F. Rapp (ed.) Herpesvirus, UCLA Symposium (new series) vol 21, Liss, Inc., New York.

10. **Drew, W.L., E. Sweet, R. Minor, and E.S. Mocarski** (1984). Multiple infections by cytomegalovirus in patients with acquired immunodeficiency syndrome: Documentation by Southern blot hybridization. **J. Infect. Diseases** 150:952-953.

11. **Mocarski, E.S., L. Deiss, and N. Frenkel** (1985). Nucleotide sequence and structural features of a novel U_S-*a* junction present in a defective herpes simplex virus genome. J. Virol. 55:140-146.

12. **Mocarski, E.S., L. Pereira, and N. Michael** (1985). Precise localization of genes on large animal virus genomes: Use of λ gtll and monoclonal antibodies to map a gene for a cytomegalovirus protein family. **Proc. Natl. Acad. Sci. USA** 82:1266-1270.

13. **Spaete, R.R. and E. S. Mocarski** (1985). The *a* sequence of the cytomegalovirus genome functions as a cleavage/packaging signal for herpes simplex virus defective genomes. **J. Virol.** 54:817-824.

14. **Spaete, R.R., and E.S. Mocarski** (1985). Regulation of cytomegalovirus gene expression: α and β promoters are trans-activated by viral functions in permissive human fibroblasts. **J. Virol.** 56:135-143.

15. **Geballe, A.P., F. L. Leach, and E.S. Mocarski** (1986). Regulation of cytomegalovirus late gene expression: λ genes are controlled by posttranscriptional events. **J. Virol.** 57:864-874.

16. **Fiala, M.D., L. A. Cone, C-M. Chang, and E.S. Mocarski** (1986). Cytomegalovirus viremia increases with progressive immune deficiency in patients infected with HTLV-III. **AIDS Research** 2:175-181.

17. **Geballe, A.P., R.R. Spaete, and E.S. Mocarski** (1986). A cis-acting element within the 5' leader of a cytomegalovirus β transcript determines kinetic class. **Cell** 46:865-872.

18. **Elias, P., M.E. O'Donnell, E.S. Mocarski and I.R. Lehman** (1986). A DNA binding protein specific for an origin of replication of herpes simplex virus type 1. **Proc. Natl. Acad. Sci. USA** 83:6322-6326.

19. **Mocarski, E.S., A.C. Liu, and R.R. Spaete** (1987). Structure and variability of the α sequence in the genome of human cytomegalovirus (Towne strain). **J. Gen. Virol.** 68:2223-2230.

20. **Spaete R.R. and E.S. Mocarski** (1987). Insertion and deletion mutagenesis of the human cytomegalovirus genome. **Proc. Natl. Acad Sci. USA** 84:7213-7217.

21. **Kemble, G.W., A.L. McCormick, L. Pereira and E.S. Mocarski** (1987). A cytomegalovirus protein with properties of herpes simplex virus ICP8: Partial purification of the polypeptide and map position of the gene. **J. Virol.** 61:3143-3151.

22 **Mocarski, E.S., W.C. Manning and J.M. Cherrington** (1988). Recombinant cytomegalovirus-based expression vectors. In: Y. Gluzman and S.H. Hughes (eds.) Viral Vectors Cold Spring Harbor Press. pp. 78-84.

23. **Ho, D. and E.S. Mocarski** (1988). β-galactosidase as a marker in peripheral and neural tissues of the herpes simplex virus infected mouse. **Virology** 167:279-283.

24. **Geballe, A.P. and E.S. Mocarski** (1988). Translational control of cytomegalovirus gene expression is mediated by upstream AUG codons. **J. Virol.** 62:3334-3340.

25. **Manning, W.C. and E.S. Mocarski** (1988). Insertional mutagenesis of the murine cytomegalovirus genome: One prominent α gene (ie2) is dispensable for growth. **Virology** 167:477-484.

26. **Nasseri, M.F. and E.S. Mocarski** (1988). The cleavage recognition signal is contained within sequences surrounding an *a-a* junction in herpes simplex virus DNA. **Virology** 167:25-30.

27. **Crute, J.J., E.S. Mocarski and I.R. Lehman** (1988). A DNA helicase induced by herpes simplex virus type 1. Nucl. Acids Res. 16:6585-6596.

28. **Mocarski, E.S., L. Pereira and A.L. McCormick** (1988). Human cytomegalovirus ICP22, the product of the HWLF1 reading frame, is an early nuclear protein that is released from cells. **J. Gen. Virol.** 69:2613-2621.

29. **Cherrington, J.M. and E.S. Mocarski** (1989). Human cytomegalovirus ie1 transactivates the α promoter-enhancer via an 18-base-pair repeat element. **J. Virol.** 63:1435-1440.

30. **Karlin, S., B.E. Blaisdell, E.S. Mocarski and V. Brendel** (1989). A method to identify distinctive charge configurations in protein sequences, with application to human herpesvirus polypeptides. **J. Mol. Biol.** 205:164-178.

31. **Crute, J.J., T. Tsurimi, S.K. Weller, M.D. Challberg, E.S. Mocarski and I.R. Lehman** (1989). The herpes simplex virus helicase-primase consists of three proteins encoded by the UL5, UL8 and UL52 genes. **Proc. Natl. Acad. Sci. USA** 86: 2186-2189.

32. **Ripalti, A., M.P. Landini, E.S. Mocarski and M. La Placa** (1989). Identification and preliminary use of recombinant λ gtll fusion proteins in cytomegalovirus diagnosis. **J. Gen. Virol.** 70:1247-1251.

33. **Leach, F.S. and E.S. Mocarski** (1989). Regulation of cytomegalovirus late gene expression: Differential use of three start sites in the transcriptional activation of ICP36 gene expression. **J. Virol** 63:1783-1791.

34. **Kemble, G.W. and E.S. Mocarski** (1989). A host cell protein binds to a highly conserved sequence element (pac-2) within the cytomegalovirus *a* sequence. **J. Virol.** 63:4715-4728.

35. **Ho, D. and E.S. Mocarski** (1989). Herpes simplex virus latent RNA (LAT) is not required for latent infection in the mouse. **Proc. Natl. Acad. Sci. USA** 86:7596-7600.

36. **Sambucetti, L.C., J.M. Cherrington, G.W.G. Wilkinson and E.S. Mocarski** (1989). NF-κB activation of the cytomegalovirus enhancer is mediated by a viral transactivator and by T cell stimulation. **EMBO J.** 8:4251-4258.

37. **Casareale, D., M. Fiala, C.M. Chang, L.A. Cone and E.S. Mocarski** (1989). Cytomegalovirus enhances lysis of HIV-infected T lymphoblasts. **Int. J. Cancer** 44:124-130.

38. **Cherrington, J.M., E. Khoury and E.S. Mocarski** (1991). Human cytomegalovirus *ie*2 negatively regulates α gene expression via a short target sequence near the transcription start site. **J. Virol.** 65:887-896.

39. **Schachtel, G.A., P. Bucher, E.S. Mocarski, B.E. Blaisdell and S. Karlin** (1991). Evidence for selective evolution in codon usage in conserved amino acid segments of human alphaherpesvirus proteins. **J. Mol. Evol.** 33:483-494.

40. **Stasiak, P.C. and E.S. Mocarski** (1991). Transactivation of a cytomegalovirus γ gene promoter requires TRS1, a member of the US22 family. In M. P. Landini (ed.) Progress in Cytomegalovirus Research, Elsevier Science Publishers, Amsterdam. 63-79.

41. **Ripalti, A. and E.S. Mocarski** (1991). The products of human cytomegalovirus genes UL1-UL7, including gp48, are dispensable for growth in cell culture. In M. P. Landini (ed.) Progress in Cytomegalovirus Research, Elsevier Science Publishers, Amsterdam. 57-60.

42. **Stasiak, P.C. and E.S. Mocarski** (1992). Transactivation of the cytomegalovirus ICP36 gene promoter requires the α gene product TRS1 in addition to IE1 and IE2. **J. Virol.** 66:1050-1058.

43. **Maciejewski, J., E. Bruening, E. Mocarski, N. Young and S. C. St Jeor** (1992). Infection of hematopoietic progenitor cells by human cytomegalovirus. **Blood** 187:170-178.

44. **Dormitzer, P.R., D.Y. Ho, E.R. Mackow, E.S. Mocarski and H. B. Greenberg** (1992). Neutralizing epitopes on herpes simplex virus-1-expressed rotavirus VP7 are dependent on coexpression of other rotavirus proteins. **Virology** 187:18-32.

45. **Dutch, R. E., R. C. Bruckner, E. S. Mocarski and I. R. Lehman** (1992). Herpes simplex virus type 1 recombination: Role of DNA replication and *a* sequences. **J. Virol.** 66:277-285.

46. **Masse, M.J., S. Karlin, G.A. Schachtel and E.S. Mocarski** (1992). Human cytomegalovirus origin of DNA replication (oriLyt) resides within a highly complex repetitive region. **Proc. Natl. Acad. Sci.** USA 89:5246-5250.

47. **Manning, W.C., C.A. Stoddart, L.A. Lagenaur, G.B. Abenes and E.S. Mocarski** (1992). Cytomegalovirus determinant of replication in salivary glands. **J. Virol.** 66:3794-3802.

48. **Bruckner, R.C., R.E. Dutch, B. Zemelman, E. S. Mocarski and I. R. Lehman** (1992) Recombination between herpes simplex virus type 1 *a* sequences. **Proc. Natl. Acad. Sci. USA** 89:10950-10954.

49. **Mocarski, E.S., M. Bonyhadi, S. Salimi, J.M. McCune and H. Kaneshima** (1993) Human cytomegalovirus in the SCID-hu mouse: Thymic epithelial cells are prominent targets of viral infection. **Proc. Natl. Acad. Sci. USA** 90:104-108

50. **Ho, D.Y., E.S. Mocarski and R. Sapolsky** (1993). Altering central nervous system physiology with a defective herpesvirus vector expressing the glucose transporter gene. **Proc. Natl. Acad. Sci. USA** 90:3655-3659.

51. **Cardin, R.D., J.M. Boname, G.B. Abenes, S.A. Jennings and E.S. Mocarski** (1993). Reactivation of murine cytomegalovirus from latency. In S. Michelson and S. A. Plotkin (ed.) Multidisciplinary Approaches to Understanding Cytomegalovirus Disease, Elsevier, Amsterdam. pp. 65-74.

52. **Boname, J.M., L.A. Lagenaur and E.S. Mocarski** (1994). Murine cytomegalovirus genes influencing virus growth and tropism for salivary gland. In Y. Becker and G. Darai (ed.) Frontiers of Virology, Vol. 3, Springer-Verlag, Heidelberg. pp. 315-328

53. **Karlin, S., E.S. Mocarski and G.A. Schachtel** (1994). Molecular evolution of herpesviruses: Genomic and protein sequence comparisons. **J. Virol.** 68:1886-1902.

54. **Vieira, J., H.E. Farrell, W.D. Rawlinson, and E.S. Mocarski** (1994). Genes in the *Hin*dIII J fragment of the murine cytomegalovirus genome are dispensable for growth in cultured cells: Insertion mutagenesis with an *lac*Z/*gpt* cassette. **J. Virol.** 68:4837-4846.

55. **Stoddart, C.A., R.D. Cardin, J.M. Boname, W.C. Manning, G.B. Abenes and E.S. Mocarski** (1994). Peripheral blood mononuclear phagocytes mediate dissemination of murine cytomegalovirus. **J. Virol.** 68:6243-6253.

56. **Kondo, K., H. Kaneshima, and E.S. Mocarski** (1994). Human cytomegalovirus latent infection of granulocyte-macrophage progenitors. **Proc. Natl. Acad. Sci. USA** 91:11879-11883.

57. **Jenkins, D.E., C.L. Martens and E.S. Mocarski** (1994). Human cytomegalovirus late protein encoded by ie2: a trans-activator as well as a repressor of gene expression. J. **Gen. Virol** 75:2337-2348.

58. **Lagenaur, L.A., W.C. Manning, J. Vieira, C.L. Martens and E.S. Mocarski** (1994). The structure and function of the murine cytomegalovirus *sgg*1 gene: A determinant of viral growth in salivary gland acinar cells. **J. Virol.** 68:7717-7727.

59. **Brown, J.M., H. Kaneshima and E.S. Mocarski.** (1995) Dramatic interstrain differences in the replication of human cytomegalovirus in SCID-hu mice. **J. Infect. Dis.** 171:1599-1603.

60. **Cardin, R.D., G.B. Abenes, C.A. Stoddart and E.S. Mocarski.** (1995) Murine cytomegalovirus IE2, an activator of gene expression, is dispensable for growth and latency in mice. **Virology** 209:236-241.

61. **Greaves, R.F., J.M. Brown, J. Vieira and E.S. Mocarski.** (1995) Selectable insertion and deletion mutagenesis of the human cytomegalovirus genome using the *E. coli* guanosine phosphoribosyl transferase (*gpt*) gene. **J. Gen. Virol.** 76:2151-2160

62. **Kondo, K., and E.S. Mocarski** (1995) Cytomegalovirus latency and latency-specific transcription in hematopoietic progenitors. **Scand. J. Infect. Dis.** (Suppl) 99:63-67.

63. **Cha, T-A., E. Tom, G.W. Kemble, G.M. Duke, E.S. Mocarski and R.R. Spaete** (1996) Human cytomegalovirus clinical isolates carry at least 19 genes not found in laboratory strains. **J. Virol.** 70:78-83.

64. **Prichard, M.N., G.M. Duke and E.S. Mocarski** (1996) Human cytomegalovirus uracil DNA glycosidase is required for the normal temporal regulation of both DNA synthesis and viral replication. **J. Virol.** 70:3018-3025.

65. **Kondo, K., J. Xu and E.S. Mocarski** (1996) Human cytomegalovirus latency-specific gene expression in granulocyte-macrophage progenitors in culture and in healthy seropositive individuals. **Proc. Natl. Acad. Sci. USA** 93:11137-11142.

66. **Mocarski, E.S., G.W. Kemble, J.M. Lyle and R.M. Greaves** (1996) A deletion mutant in the human cytomegalovirus gene encoding $IE1_{491aa}$ is replication defective due to a failure in autoregulation. **Proc. Natl. Acad. Sci. USA** 93:11321-11326.

67. **Dittmer, D. and E.S. Mocarski** (1997) Human cytomegalovirus infection inhibits G_1/S transition. J. Virol. 71:1629-1634.

68. **Lowry, P.W., C.S. Koropchak, C.Y.H. Choi, E.S. Mocarski, E.R. Kern, P.R. Kinchington and A.M. Arvin** (1997) The synthesis and immunogenicity of varicella-zoster virus glycoprotein E and immediate-early protein (IE62) expressed in recombinant herpes simplex virus-1. **Antiviral Res.** 33:187-200.

69. **Masse, M.J., M. Messerle and E.S. Mocarski** (1997) The location and sequence composition of the murine cytomegalovirus replicator (*ori*Lyt). **Virology** 230:350-360.

70. **Mocarski, E.S., M.N. Prichard, C.S. Tan and J.M. Brown** (1997) Reassessing the organization of the UL42-UL43 region of the human cytomegalovirus strain AD169 genome. **Virology** 239:169-175.

71. **Penfold, M.E.T, and E.S. Mocarski** (1997) Formation of cytomegalovirus DNA replication compartments defined by localization of viral proteins and DNA synthesis. **Virology** 239:46-61.

72. **Greaves, R. F., and E.S. Mocarski** (1998) Low multiplicity growth defect and gene expression during infection by a human cytomegalovirus *ie*1 mutant. **J. Virol.** 72:366-379.

73. **McVoy, M.A., D.E. Nixon, S.P. Adler, and E.S. Mocarski** (1998) Sequences within the herpesvirus-conserved *pac*1 and *pac*2 motifs are required for cleavage and packaging of the murine cytomegalovirus genome. **J. Virol.** 72:48-56.

74. **Hahn, G., R. Jores and E.S. Mocarski** (1998) Cytomegalovirus latency in a common precursor of dendritic and myeloid cells. **Proc. Natl. Acad. Sci. USA** 95:3937-3942.

75. **Leong, C.C., T.L. Chapman, P.J. Bjorkman, D. Formankova, E.S. Mocarski, J.H. Phillips and L.L. Lanier** (1998) Modulation of natural killer cell cytotoxicity in human cytomegalovirus infection: The role of endogenous class I MHC and a viral class I homolog. **J. Exp. Med.** 187:1681-1687.

76. **Reichenspurner, H., V. Soni, M. Nitschke, G.J. Berry, T. Brazelton, R. Shorthouse, X. Huang, J. Boname, R. Girgis, B.A. Raitz, E. Mocarski, Sandford, G. and R.E. Morris** (1998) Enhancement of obliterative airway disease in rat tracheal allografts infected with recombinant rat cytomegalovirus. **J. Heart Lung Transplant.** 17:439-451.

77. **Bolovan-Fritts, C.A., E.S. Mocarski and J.A. Wiedeman** (1999) Peripheral blood CD14+ cells from healthy subjects carry a circular conformation of latent cytomegalovirus genome. **Blood** 93:394-398.

78. **Slobedman, B., and E.S. Mocarski** (1999) Quantitative analysis of latent human cytomegalovirus. **J. Virol.** 73:4806-4812

79. **Penfold, M.E.T., D.J. Dairaghi, G. M. Duke, N. Saederup, E.S. Mocarski, G.W. Kemble and T.J. Schall** (1999) Cytomegalovirus encodes a potent α chemokine. **Proc. Natl. Acad. Sci.** USA 96:9839-9844.

80. **McVoy, M.A., and E.S. Mocarski** (1999) Tetracycline-mediated regulation of gene expression within the human cytomegalovirus genome. **Virology** 258: 295-303.

81. **Saederup, N., Y.C. Lin, D.J. Dairaghi, T.J. Schall and E.S. Mocarski** (1999) Cytomegalovirus-encoded beta chemokine promotes monocyte-associated viremia in the host. **Proc. Natl. Acad. Sci. USA** 96: 10881-10886.

82. **Goldmacher, V.S., L.M. Bartle, A. Skaletskaya, C.A. Dionne, N.L. Kedersha, C.A. Vater, J.W. Han, R.J. Lutz, S. Watanabe, E.D. McFarland, E.D. Kieff, E.S. Mocarski and T. Chittenden.** (1999) A cytomegalovirus mitochondria-localized inhibitor of apoptosis structurally unrelated to Bcl-2. **Proc. Natl. Acad. Sci. USA** 96: 12536-12541.

83. **van den Pol, A.N., E.S. Mocarski, N. Saederup, J. Vieira and T.J. Meier.** (1999) Cytomegalovirus cell tropism, replication and gene transfer in brain. **J. Neuroscience** 19:10948-10965.

84. **Landini, M.P., T. Lazzarotto, J. Xu, A. Geballe and E.S. Mocarski.** (2000) Humoral response to proteins of human cytomegalovirus latent transcripts. **Biol. Blood Marrow Transplant** 6:100-108.

85. **White, K.L., B. Slobedman, J. Xu and E.S. Mocarski.** (2000) Human cytomegalovirus latency-associated protein pORF94 is dispensable for productive and latent infection. **J. Virol.** 74:9333-9337.

86. **Wolf, D.G., C. Tan Courcelle, M.N. Prichard and E.S. Mocarski.** (2001) Distinct and separate roles for herpesvirus-conserved UL97 kinase in cytomegalovirus DNA synthesis and encapsidation. **Proc. Natl. Acad. Sci. USA** 98:1895-1900.

87. **Courcelle, C.T., J. Courcelle, M.N. Prichard and E.S. Mocarski.** Cytomegalovirus requires uracil-DNA glycosylase activity for transition to late phase viral DNA replication. (2001) J. Virol. 75:7592-7601.

88. **Skaletskaya, A., L.M. Bartle, T. Chittenden, A.L. McCormick, E.S. Mocarski and V.S. Goldmacher.** (2001) A cytomegalovirus-encoded inhibitor of apoptosis that suppresses caspase-8 activation. **Proc. Natl. Acad. Sci. USA** 98:7829-7834.

89. **Roback, J.D., C.D. Hillyer, W.L. Drew, M. Laycock, J. Luka, E.S. Mocarski, B. Slobedman, J.W. Smith, C. Soderberg-Naucler, D. Todd, S. Woxenius, and M.P. Busch.** (2001) Multicenter evaluation of PCR methodologies to detect cytomegalovirus DNA in blood donors. **Transplantation** 41:1249-1257.

90. **Saederup, N., S.A. Aguirre, T.E. Sparer, D.M. Bouley and E.S. Mocarski.** (2001) Murine cytomegalovirus CC chemokine homolog MCK-2 (m131-129) is a determinant of dissemination that increases inflammation at initial sites of infection. J. Virol. 75:9966-9976.

91. **Arase, H., E.S. Mocarski, A.E. Campbell, A.B. Hill and L.L. Lanier** (2002) Direct recognition of cytomegalovirus by activating and inhibitory NK cell receptors. **Science** 296:1323-1326

92. **Slobedman, B., E.S. Mocarski, A.M. Arvin, E. Mellins and A. Abendroth.** (2002) Latent human cytomegalovirus downregulates major histocompatibility complex class II expression on myeloid cells. **Blood** 100:2867-2873.

93. **Carr, W.H., A.M. Little, E.S. Mocarski, and P. Parham.** (2002) NK-Cell Mediated Lysis of Autologous HCMV Infected Skin Fibroblasts Is Highly Variable Among NK-Cell Clones and Polyclonal NK-Cell Lines. **Clin. Immunology** 105:126-140.

94. **McCormick, A.L., V.L. Smith, D. Chow, and E.S. Mocarski.** (2003) Disruption of mitochondrial networks by human cytomegalovirus *UL37* gene product vMIA. **J. Virol.** 77:631-641.

95. **Hertel, L., V.G. Lacaille, H. Strobl, E.D. Mellins, and E.S. Mocarski.** (2003) Susceptibility of immature and mature Langerhans cell-type dendritic cells to infection and immunomodulation by human cytomegalovirus. **J. Virol.** 77:7563-7574.

96. **Lodoen M., K. Ogasawara, J.A. Hamerman, H. Arase, J.P. Houchins, E.S. Mocarski, L.L. and Lanier.** (2003) NKG2D-mediated NK cell protection against cytomegalovirus is impaired by viral gp40 modulation of RAE-1 molecules. **J. Exp. Med.** 197:1245-1253.

97. **Arber, C., A. BitMansour, T.E. Sparer, J.P. Higgins, E.S. Mocarski, I.L. Weissman, J.A. Shiziru, and J.M.Y. Brown.** (2003) Common lymphoid progenitors rapidly engraft and protect against lethal cytomegalovirus infection after hematopoietic cell transplantation. **Blood** *102*:421-428.

98. **McCormick, A.L., A Skaletskaya, P.A. Barry, E.S. Mocarski, and V.S. Goldmacher.** (2003) Differential function and expression of the viral inhibitor of caspase 8-induced apoptosis (vICA) and the viral mitochondrial-localized inhibitor of apoptosis (vMIA) cell death suppressors conserved in primate and rodent cytomegaloviruses. **Virology** 316:221-233.

99. **Weis, M., T.N. Kledal, K.Y. Lin, S.N. Panchal, S.Z. Gao, H.A. Valantine, E.S. Mocarski, and J.P. Cooke.** (2004) Cytomegalovirus infection impairs the nitric oxide pathway: Role of ADMA in transplant arteriosclerosis. **Circulation** 109:500-505.

100 **Slobedman, B., J.L. Stern, A.L. Cunningham, A. Abendroth, E.S. Mocarski.** (2004). Impact of human cytomegalovirus latent infection on myeloid progenitor cell gene expression. **J. Virol.** 78:4054-4062.

101. **Sparer, T.E., J. Gosling, T.J. Schall, and E.S. Mocarski.** (2004) Expression of human CXCR2 in murine neutrophils as a model for assessing cytomegalovirus chemokine vCXCL-1 function *in vivo.* **J. Interferon Cyto Res** (submitted for publication).

102. **Abate, D.A., S. Watanabe, and E.S.Mocarski.** (2003) Major human cytomegalovirus structural protein pp65 (ppUL83) blocks the IRF-3-dependent interferon response. **J. Virol.** (submitted for publication)

103. **Hertel, L., S. Watanabe, and E.S. Mocarski** (2004) Global analysis of cytomegalovirus gene expression at late times during infection reveals extensive dysregulation of cell cycle gene expression and induction of pseudomitosis independent of US28 function. **J. Virol.** (submitted for publication).

Invited Reviews, Commentaries and Chapters:

Mocarski, E.S. (1988). Biology and Replication of Cytomegalovirus. Transfusion Medicine Reviews 2:229-234.

Mocarski, E.S. (1988). A meeting review. Genes & Development 2:926-928.

Mocarski, E.S., G. B. Abenes, L. C. Sambucetti, W. C. Manning and J. M. Cherrington (1990). Molecular genetic analysis of cytomegalovirus gene function in growth, persistence and latency. Curr. Topics Micro. Immunol. 154:47-74.

Mocarski, E.S. (1991). Evidence for posttranscriptional regulation of cytomegalovirus gene expression. In E. Wagner, (ed.) Herpesvirus Transcription and Its Regulation CRC Reviews in Biology. CRC Press, Boca Raton, pp 287-299.

Mocarski, E.S. (1991). Initial events involved in CMV-cell interactions. Transplantation Proceedings 23:43-47.

Mocarski, E.S. (1993). Cytomegalovirus biology and replication. In B. Roizman, R. J. Whitley, C. Lopez (eds.) The Human Herpesviruses. Raven Press, New York. pp 173-226.

Mocarski, E.S. (1994) Cytomegalovirus. In R. Webster, A. Granoff (eds.) Encyclopedia of Virology. Saunders Scientific Publications, London.

Mocarski, E.S. (1995) Cytomegaloviruses and their replication. In B. N. Fields, D. M. Knipe, P. M. Howley (eds.) Fields Virology. Lippincott-Raven Publishers, New York. pp. 2447-2492.

Mocarski, E.S. and G.W. Kemble (1997) Recombinant cytomegaloviruses for study of replication and pathogenesis. Intervirology 39:320-330.

Mocarski. E.S. (1997) Propagation of KSHV in cultured cells (editorial). N. Eng. J. Med. 336:214-215.

Kemble, G.W., G.M. Duke and E.S. Mocarski (1999) Human cytomegalovirus infection of the SCID-hu (thy/liv) mouse. Handbook of Animal Models of Infection. Academic Press.

Mocarski, E.S. (1999) Cytomegalovirus. In R. Webster, A. Granoff (eds.) Encyclopedia of Virology. Saunders Scientific Publications, London. Volume 1, pages 344-351.

Mocarski, E.S., and C.T. Courcelle (2001) Cytomegaloviruses and their replication. In D. M. Knipe, P. M. Howley (Eds.) Fields Virology. Lippincott Williams & Wilkins, Philadelphia. pp 2629-2673.

Saederup, N., and E.S. Mocarski (2002) Fatal Attraction: Cytomegalovirus-encoded chemokine homologs. Curr. Top. Microbiol. Immunol. 269: 235-256

Mocarski, E.S. (2002) Virus self-improvement through inflammation: No pain, no gain. Proc. Natl. Acad. Sci. USA 99: 3362-3364

Mocarski, E.S. (2002) Immunomodulation by cytomegalovirus: manipulative strategies beyond evasion. Trends Microbiol 10:332-339

Patents:

Ho, D.Y-W., R.M. Sapolsky, E.S. Mocarski (1992) Gene transfer using herpes virus vectors as a tool for neuroprotection. U.S. Patent No. 5,661,033.

Mocarski, E. S. and K. Kondo (1995). Latent transcripts and proteins of cytomegalovirus. U.S.Patent No. 5,783,383.

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PATENT
Attorney Docket No.: 019934-000310US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 9088
Thomas J. Schall, et al.	Examiner: Jiang, S. Anna
Application No.: 09/944,163	Technology Center/Art Unit: 1617
Filed: August 30, 2001	
For: MODULATORS OF US 28	Declaration of Brian E. McMaster under 37 C.F.R. § 1.132
Customer No.: 20350	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Brian E. McMaster being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 U.S.C. § 1001), and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true, and statements made on information or belief are believed to be true and correct.

2. I am a named inventor of the above-referenced application.

3. I am presently employed as a researcher at ChemoCentryx in a high through put screening laboratory.

4. I understand that the general ability of neuroleptics to bind the US28 receptor is an issue bearing on the patentability of the presently claimed subject matter. I present additional information bearing on this question. All the work described herein was either conducted by me, at my direction, or by my colleagues who work with me as part of the team of scientists working on this project.

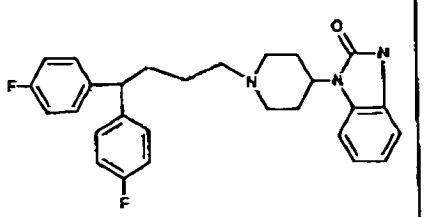
5. As set forth in the specification, we have found octoclothepin and methiothepin to be ligands for the CMV US28 receptor. We have also examined the activity of the other psychotropic agents (e.g., dopamine receptor antagonists or serotonin receptor antagonists) as set forth in Appendix A (i.e., Spiperone, Metoclopramide, Domperidone, Pimozide, Risperidone, Raclopride, and Sulpiride). None of these other agents were appreciably active as ligands of the CMV US28 receptor.

The declarant has nothing further to say.

Brian E. McMaster

5/14/2004
Date

STRUCTURE

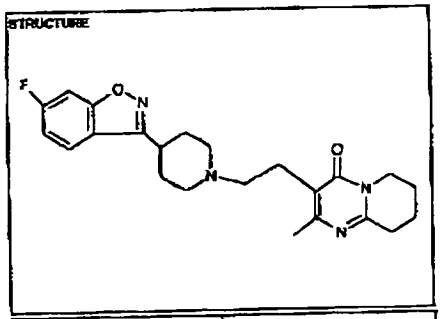


ID	location
P-100	RK004-A9
formula: $C_{28}H_{29}F_2N_3O$	MW: 461.6
Class: Dopamine	Action: Antagonist

LOPAC Structures and Description

Description
Ca2+ channel antagonist; antipsychotic; D2 dopamine receptor antagonist
Selectivity: D2
Name
Pimozide

STRUCTURE

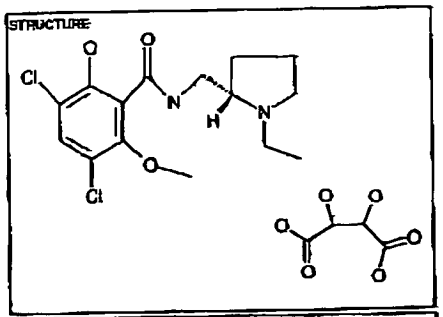


ID	location
R-118	RK004-B10
formula: $C_{23}H_{27}FN_4O_2$	MW: 410.5
Class: Dopamine	Action: Antagonist

LOPAC Structures and Description

Description
D2 Dopamine receptor antagonist; 5-HT2 serotonin receptor antagonist; antipsychotic
Selectivity: D2
Name: R 62 766
Risperidone

STRUCTURE

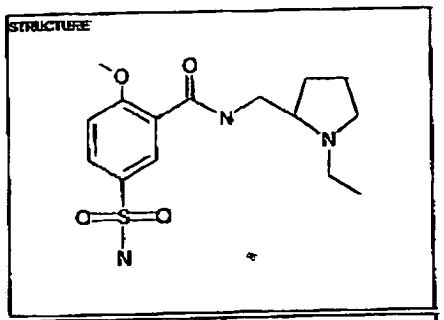


ID	location
R-121	RK004-C10
formula: $C_{19}H_{25}Cl_2N_2O_9$	MW: 497.3
Class: Dopamine	Action: Antagonist

LOPAC Structures and Description

Description
Selective D2 dopamine receptor antagonist
Selectivity: D2
Name
S(+)-Raclopride L-tartrate

STRUCTURE



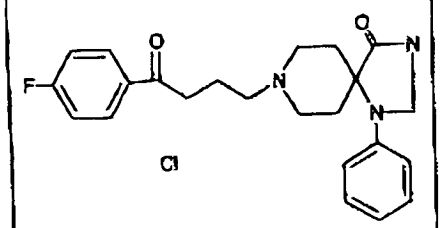
ID	location
S-116	RK004-E10
formula: $C_{15}H_{23}N_3O_4S$	MW: 341.4
Class: Dopamine	Action: Antagonist

LOPAC Structures and Description

Description
D2 Dopamine receptor antagonist; antipsychotic
Selectivity: D2
Name: (±)-5-(Aminosulfonyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-2-methoxybenzamide
(±)-Sulpiride

APPENDIX A

STRUCTURE

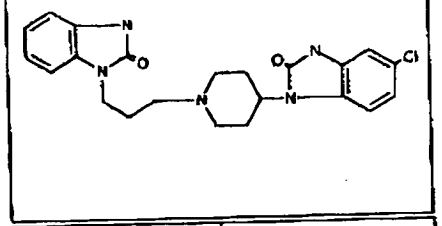


ID	location
D-050	RK004-H5
formula $C_{23}H_{27}ClFN_3O_2$	MW 431.9
Class Dopamine	Action Antagonist

LOPAC Structures and Description

Description
Selective antagonist for D2 dopamine receptor
Selectivity D2
Name RI 5147 hydrochloride; Spiroperidol hydrochloride
Spiperone hydrochloride

STRUCTURE

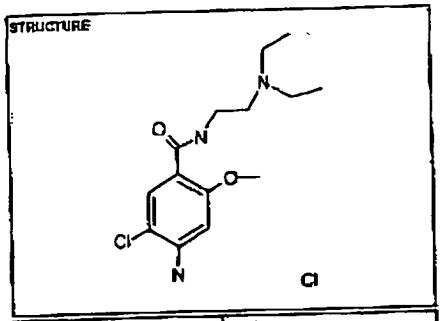


ID	location
D-122	RK004-C6
formula $C_{22}H_{24}ClN_5O_2$	MW 425.9
Class Dopamine	Action Antagonist

LOPAC Structures and Description

Description
Peripheral dopamine receptor antagonist that does not cross the blood-brain barrier; anti-emetic
Selectivity D2
Name
Domperidone

STRUCTURE

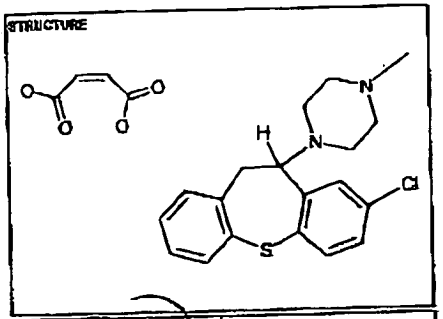


ID	location
M-117	RK004-D8
formula $C_{14}H_{23}Cl_2N_3O_2$	MW 336.3
Class Dopamine	Action Antagonist

LOPAC Structures and Description

Description
5-HT3 Serotonin receptor antagonist; D2 dopamine receptor antagonist; anti-emetic
Selectivity D2
Name
Metoclopramide hydrochloride

STRUCTURE



ID	location
O-111	RK004-G8
formula $C_{23}H_{25}ClN_2O_4S$	MW 461.0
Class Dopamine	Action Antagonist

LOPAC Structures and Description

Description
D2 Dopamine receptor antagonist; serotonin receptor antagonist
Selectivity D2
Name 1-(8-Chloro-10,11-dihydrobenzo[b,f]thiepin-10-yl)-4-methyl-piperazine maleate
(±)-Octoclothepin maleate

O-111

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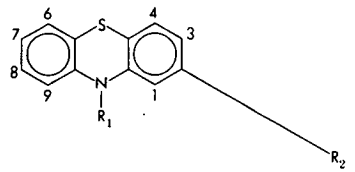
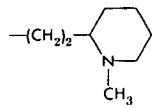
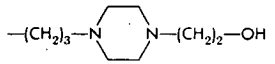
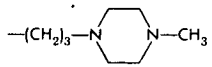
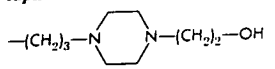
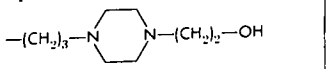
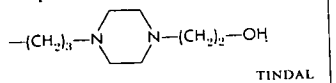
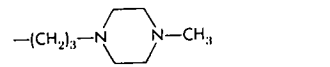
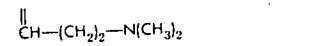
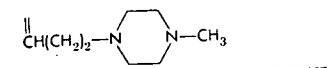
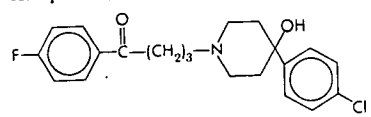
Table 12-2. SELECTED ANTIPSYCHOTIC DRUGS: CHEMICAL STRUCTURES, DOSES, SIDE EFFECTS, AND DOSAGE FORMS

NONPROPRIETARY NAME / TRADE NAME		DOSE			SIDE EFFECTS			DOSAGE FORMS		
Phenothiazines		*Antipsychotic Dose Range—Daily Dosage*		*Single Intramuscular Dose †*	*Sedative Effects*	*Extrapyramidal Effects*	*Hypotensive Effects*	*Oral*		*Injection*
		Usual (mg)	Extreme * (mg)	(mg)				T = tablet (mg) C = capsule (mg)	S = syrup E = elixir C = concentrate	A = ampul V = vial S = syringe
Chlorpromazine Hydrochloride, U.S.P. $-(CH_2)_3-N(CH_3)_2$ THORAZINE	—Cl	200–800	25–2000	25–50	+++	++	I.M. +++ Oral ++	(T) 10, 25, 50, 100, 200 (C) sustained release; 30, 75, 150, 200, 300	(S) 10 mg/5 ml (C) 30 mg/ml, 100 mg/ml ‡	(A) 25 mg/ml, 50 mg/2 ml (V) 25 mg/ml in 10 ml
Triflupromazine Hydrochloride, N.F. $-(CH_2)_3-N(CH_3)_2$ VESPRIN	$-CF_3$	50–200	50–400	20–50	++	+++	++	(T) 10, 25, 50	(S) 50 mg/5 ml	(V) 10 mg/ml in 10 ml (S) 10 mg/ml
Thioridazine Hydrochloride, U.S.P.  MELLARIL	$-SCH_3$	100–600	50–800		+++	+	++	(T) 10, 25, 50, 100, 150, 200	(C) 30 mg/ml	
Perphenazine, N.F.  TRILAFON	—Cl	8–32	4–64	5–10	++	+++	+	(T) 2, 4, 8, 16 (T) sustained release; 8	(S) 2 mg/5 ml (C) 16 mg/5 ml	(A) 5 mg/ml (V) 5 mg/ml
Prochlorperazine Edisylate, U.S.P. Prochlorperazine Maleate, U.S.P.  COMPAZINE (EDISYLATE AND MALEATE)	—Cl	75–100	15–150	5–10	++	+++	+	(T) 5, 10, 25 (C) sustained release; 10, 15, 30, 75	(S) 5 mg/5 ml (C) 10 mg/ml ‡	(A) 5 mg/ml
Fluphenazine Hydrochloride, U.S.P. ***Fluphenazine Enanthate, U.S.P.*** Fluphenazine decanoate  PERMITIL, PROLIXIN (HYDROCHLORIDE, ENANTHATE, AND DECANOATE)	$-CF_3$	2–10	1–25	1.25–4 (decanoate or enanthate: 25–50 every 2 weeks)	+	+++	+	(T) 0.25, 1, 2.5, 5, 10 (T) sustained release; 1	(C) 5 mg/ml (E) 0.5 mg/ml	(V) 2.5 mg/ml in 10 ml, enanthate and decanoate (S) 25 mg/ml (V) 25 mg/ml in 5 ml
Acetophenazine Maleate, N.F.	$-COCH_3$	40–80	20–150		++	++	+	(T) 20		

Fluphenazine Hydrochloride, U.S.P. *Fluphenazine Enanthate, U.S.P.* *Fluphenazine decanoate*  PERMITIL, PROLIXIN (HYDROCHLORIDE, ENANTHATE, AND DECANOATE)	$-CF_3$	2–10	1–25	1.25–4 (decanoate or enanthate: 25–50 every 2 weeks)	+	+++	+	(T) 0.25, 1, 2.5, 5, 10 (T) sustained release; 1	(C) 5 mg/ml (E) 0.5 mg/ml	(V) 2.5 mg/ml in 10 ml, enanthate and decanoate (S) 25 mg/ml (V) 25 mg/ml in 5 ml
Acetophenazine Maleate, N.F.  TINDAL	$-COCH_3$	40–80	20–150		++	++	+	(T) 20		
Trifluoperazine Hydrochloride, N.F.  STELAZINE	$-CF_3$	4–15	2–64	1–2	+	+++	+	(T) 1, 2, 5, 10	(C) 10 mg/ml	(V) 2 mg/ml in 10 ml
Thioxanthenes §										
Chlorprothixene, N.F.  TARACTAN	—Cl	50–400	30–600	25–50	+++	++	++	(T) 10, 25, 50, 100	(C) 100 mg/5 ml	(A) 25 mg/2 ml
Thiothixene Hydrochloride, N.F.  NAVANE	$-SO_2N(CH_3)_2$	6–30	6–60	2–6	+ to ++	++	++	(C) 1, 2, 5, 10, 20 ‡	(C) 5 mg/ml	(A) 4 mg/2 ml
Butyrophenones										
Haloperidol, U.S.P.  HALDOL		2–6	1–30	3–5	+	+++	+	(T) 0.5, 1, 2, 5	(C) 2 mg/ml	(A) 5 mg/ml

* Extreme dosage ranges should not be exceeded except when all other appropriate measures have failed.

† Except for the enanthate and decanoate forms of fluphenazine, dosage is given I.M. every 4 to 6 hours for agitated patients.

‡ Chlorpromazine, U.S.P., is available as the free base in rectal suppositories in 25- and 100-mg sizes; Prochlorperazine, U.S.P., suppositories contain 2.5, 5, or 15 mg of the free base; Thiothixene, N.F., is available as the free base in 1-, 2-, 5-, and 10-mg capsules.

§ C= replaces N at position 10 in the general formula of phenothiazines (*see* structure at top of first column).

THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

TENTH EDITION

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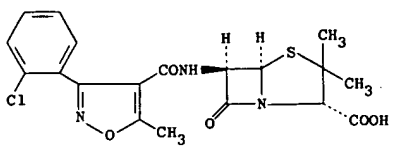
2375. Clove. Caryophyllus. Dried flower-buds of *Eugenia caryophyllata* Thunb. *(Caryophyllus aromaticus* L.), *Myrtaceae. Habit.* Molucca Islands, Zanzibar, Sumatra, S. America, W. Indies. *Constit.* 15-18% eugenol, caryophyllin, tannin, gum, resin.

USE: Manuf oil of clove, eugenol; in baking; confections.
THERAP CAT: Dental analgesic, pharmaceutic aid (flavor).

2376. Cloxacillin. *6-[[[3-(2-Chlorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid;* [3-(*o*-chlorophenyl)-5-methyl-4-isoxazolyl]penicillin; [5-methyl-3-(*o*-chlorophenyl)-4-isoxazolyl]penicillin; 6-[3-(*o*-chlorophenyl)-5-methyl-4-isoxazolecarboxamido]penicillanic acid. $C_{19}H_{18}ClN_3O_5S$; mol wt 435.88. C 52.36%, H 4.16%, Cl 8.13%, N 9.64%, O 18.35%, S 7.35%. Prepn: Doyle *et al., J. Chem. Soc.* **1963,** 5838. Manuf: *Ind. Chem.* **39,** 513 (1963), *C.A.* **60,** 1543a (1964). Properties and pharmacology: Naylor *et al., Nature* **195,** 1264 (1962). Comprehensive description: D. L. Mays in *Analytical Profiles of Drug Substances* **vol. 4,** K. Florey, Ed. (Academic Press, New York, 1975) pp 113-136.

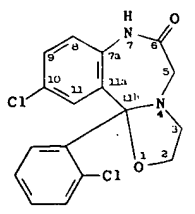


Sodium monohydrate, $C_{19}H_{17}ClN_3NaO_5S.H_2O$, *sodium cloxacillin, BRL-1621, Bactopen, Cloxapen, Cloxypen, Ekvacillin, Gelstaph, Orbenin, Methocillin-S, Prostaphlin-A, Staphobristol-250, Staphybiotic, Tegopen, Tepogen.* Microcryst powder, dec 170°. $[\alpha]_D^{20}$ +163°. pH 6.0-7.5. Sol in water, methanol, ethanol, pyridine, ethylene glycol. LD_{50} i.p. in rats, mice: 1630 ±112, 1280 ±50 mg/kg, E. I. Goldenthal, *Toxicol. Appl. Pharmacol.* **18,** 185 (1971).

Benzathine salt, $C_{54}H_{56}Cl_2N_8O_{10}S_2$, *Boviclox, Dry-Clox, Noroclox DC, Orbenin Dry Cow, Triclox.*

THERAP CAT: Antibacterial.
THERAP CAT (VET): Antibacterial.

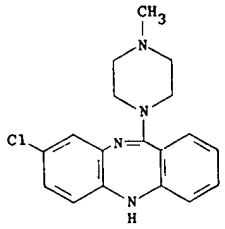
2377. Cloxazolam. *10-Chloro-11b-(2-chlorophenyl)-2,3,7,11b-tetrahydrooxazolo[3,2-d][1,4]benzodiazepin-6(5H)-one;* 7-chloro-5-(2-chlorophenyl)tetrahydrooxazolo[5,4-*b*]-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-2-one; 10-chloro-11b-(2-chlorophenyl)-2,3,5,6,7,11b-hexahydrobenzo[6,7]-1,4-diazepino[5,4-*b*]oxazol-6-one; 10-chloro-11b-(2-chlorophenyl)-6-oxo-2,3,5,6,7,11b-hexahydrooxazolo[3,2-*d*]-[1,4]benzodiazepine; CS-370; Enadel; Olcadil; Sepazon. $C_{17}H_{14}Cl_2N_2O_2$; mol wt 349.21. C 58.47%, H 4.04%, Cl 20.30%, N 8.02%, O 9.16%. Prepn: Tachikawa *et al.,* Ger. pats. **1,812,252** and **1,952,201** corresp to U.S. pats. **3,772,371** and **3,696,094** (1969, 1970, 1973, 1972, all to Sankyo); Miyadera *et al., J. Med. Chem.* **14,** 520 (1971). Pharmacology: Kamioka *et al., Arzneimittel-Forsch.* **22,** 884 (1972). Metabolism: Murata *et al., Chem. Pharm. Bull.* **21,** 404 (1973). Multicenter trials and complementary studies: K. A. Fischer-Cornelssen, *Arzneimittel-Forsch.* **31,** 1757 (1981).



Crystals, mp 202-204° (dec). Freely sol in glacial acetic acid; sparingly sol in chloroform; slightly sol in acetone, dehydrated ethanol, ethyl acetate, benzene. Practically insol in water. LD_{50} in mice: 3.3 g/kg orally; > 2.0 g/kg i.p.

THERAP CAT: Minor tranquilizer.

2378. Clozapine. *8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]diazepine;* HF 1854; Leponex; Lepotex. $C_{18}H_{19}ClN_4$; mol wt 326.83. C 66.15%, H 5.86%, Cl 10.85%, N 17.14%. Prepn: Fr. pat. **1,334,944** (1963 to Wander) corresp to Schmutz, Hunziker, U.S. pat. **3,539,573** (1970); Neth. pat. **Appl. 293,201** (1965 to Wander), *C.A.* **64,** 8221a (1966); Hunziker *et al., Helv. Chim. Acta* **50,** 1588 (1967). Structure-activity studies: Schmutz *et al., Chim. Ther.* **2,** 424 (1967). Pharmacology: Stille *et al., Farmaco, Ed. Prat.* **26,** 603 (1971). Metabolism: Gauch, Michaelis, *ibid.* 667. Toxicology: Lindt *et al., ibid.* 585. Clinical studies: De Maio, *Arzneimittel-Forsch* **22,** 919 (1972). *Review:* A. C. Sayers, H. A. Amsler, in *Pharmacological and Biochemical Properties of Drug Substances* **vol. 1,** M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1977) pp 1-31.



Yellow crystals from acetone-petr ether, mp 183-184°. uv max (ethanol): 215, 230, 261, 297 nm (ε 27,400, 25,800, 16,800, 10,500). LD_{50} in mice, rats: 61, 58 mg/kg i.v.; 199, 260 mg/kg orally, Lindt *et al., loc. cit.*

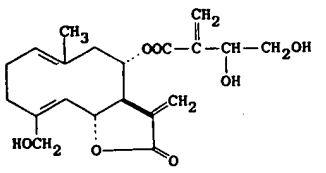
THERAP CAT: Sedative.

2379. Clupeine. Protamine found in herring *(Clupea pallasii)* sperm. Isoln from herring testes contg ripe sperm: Kossel, *The Protamines and Histones* (London, 1928); Rasmussen, *Z. Physiol. Chem.* **224,** 97 (1934); Felix, Mager, *ibid.* **249,** 111 (1937); Block *et al., Proc. Soc. Exp. Biol. Med.* **70,** 494 (1949). Separated into two main fractions, Y and Z, and fraction Y separated into Y_I and Y_{II}: Ando, Sawada, *J. Biochem. (Tokyo)* **49,** 252 (1961). Chemical structure of fraction Z: Ando *et al., Biochem. Biophys. Acta* **56,** 628 (1962); Felix, Hashimoto, *Z. Physiol. Chem.* **330,** 205 (1963). Complete amino acid sequence of Z component: Iwai *et al., J. Biochem. (Tokyo)* **69,** 493 (1971); of Y_{II} component: Suzuki, Ando, *ibid.* **72,** 1419 (1972); of Y_I component: *eidem, ibid.* 1433. Solid-phase synthesis of clupeine Z: Yonezawa *et al., C.A.* **79,** 19093k (1973).

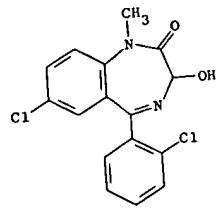
White powder, strongly alkaline reaction. pKa 7.4-8.0; pKb 2.9-3.3.

Usually isolated as the sulfate B-$2H_2SO_4$; white powder, $[\alpha]_D^{22}$ −85.49° (satd aq soln). One gram dissolves in 80 ml water at room temp. Freely sol in hot water, separates from the supersatd soln on cooling as a clear, colorless oil contg 50% H_2O, n_D^{20} 1.4435. Clupeine is split by protaminase, active trypsin and by chymotrypsin. Compds of clupeine with nucleic acids are described by Kossel, *loc. cit.*

2380. Cnicin. *3,4-Dihydroxy-2-methylenebutanoic acid 2,3,3a,4,5,8,9,11a-octahydro-10-(hydroxymethyl)-6-methyl-3-methylene-2-oxocyclodeca[b]furan-4-yl ester; 6α,8α,15-trihydroxygermacra-1(10),4,11(13)-trien-12-oic acid 12,6-lactone 8-(3,4-dihydroxy-2-methylenebutyrate);* cynisin; centaurin. $C_{20}H_{26}O_7$; mol wt 378.41. C 63.48%, H 6.93%, O 29.60%. Bitter principle of *Cnicus benedictus* L., *Compositae.* Isolation and review: Korte, Bechmann, *Naturwiss.* **45,** 390 (1958). Structure: Suchy *et al., Tetrahedron Letters* no. 10, 5 (1969); *Ber.* **93,** 2449 (1960). Revised structure: Samek *et al., Tetrahedron Letters* **1969,** 2931. Stereochemistry: Tori *et al., J. Chem. Soc. (B)* **1971,** 1084.



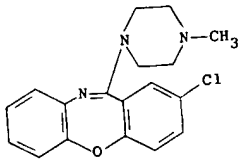
Anaesthesist **28,** 578 (1979). Comparative study: H. Ott *et al., ibid.* 29. Absorption, distribution, excretion of ^{14}C-lormetazepam: R. Girkin *et al., Xenobiotica* **10,** 401 (1980). Radioimmunologic study: M. Hümpel *et al., Clin. Pharmacol. Ther.* **28,** 673 (1980).



Cryst from ethanol/THF, mp 205-207°.

THERAP CAT: Sedative; hypnotic.

5404. Loxapine. *2-Chloro-11-(4-methyl-1-piperazinyl)-dibenz[b,f][1,4]oxazepine;* oxilapine; CL-62362; S-805; SUM-3170. $C_{18}H_{18}ClN_3O$; mol wt 327.81. C 65.95%, H 5.53%, Cl 10.81%, N 12.82%, O 4.88%. Prepn: Neth. pat. Appl. **6,406,089** corresp to Schmutz *et al.,* U.S. pat. **3,546,-226** (1964, 1970 both to Wander); *eidem, Helv. Chim. Acta* **50,** 245 (1967); Coppola, U.S. pat. **3,412,193** (1968 to Am. Cyanamid). Crystal structure: D. B. Cosulich, F. M. Lovell, *Acta Crystallogr.* **33B,** 1147 (1977). Pharmacology: Schmutz *et al., Chim. Ther.* **2,** 424 (1967); Latimer, *J. Pharmacol. Exp. Ther.* **166,** 151 (1969). Toxicity studies: Mineshita *et al., Oyo Yakuri* **4,** 293 (1970), *C.A.* **76,** 81145v (1972).



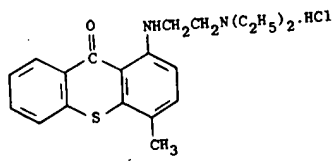
Pale yellowish crystals from petr ether, mp 109-110°. LD_{50} orally in mice: 65 mg/kg orally, Stille *et al., Arzneimittel-Forsch.* **15,** 841 (1965).

Hydrochloride, $C_{18}H_{19}Cl_2N_3O$, *Loxitane C.*

Succinate, $C_{22}H_{24}ClN_3O_5$, *CL-71563, Daxolin, Loxapac, Loxitane.*

THERAP CAT: Tranquilizer (minor).

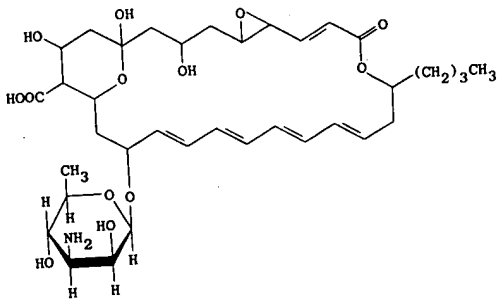
5405. Lucanthone Hydrochloride. *1-[(2-Diethylamino-ethyl)amino]-4-methylthioxanthen-9-one hydrochloride;* 1-(2-diethylaminoethylamino)-4-methylthiaxanthone hydrochloride; Ms 752; RP 3735; Miracil D; Nilodin; Miracol; Tixantone. $C_{20}H_{25}ClN_2OS$; mol wt 376.94. C 63.72%, H 6.69%, Cl 9.41%, N 7.43%, O 4.24%, S 8.51%. Prepd by the reaction of 1-chloro-4-methylthiaxanthone with *asym*-diethylethylenediamine: Mauss, *Naturwiss.* **33,** 253 (1946); *idem, Ber.* **81,** 19 (1948); Sharp, *J. Chem. Soc.* **1951,** 2961; Archer, Suter, *J. Am. Chem. Soc.* **74,** 4296 (1952). Review of mode of action: Weinstein, Hirschberg, *Progr. Mol. Subcell. Biol.* **2,** 232 (1971). *Review:* Hirschberg in *Antibiotics* vol. **3,** J. W. Corcoran, F. E. Hahn, Eds. (Springer-Verlag, New York, 1975) pp 274-303.



Yellow crystals from alcohol, mp 195-196° (free base mp 64-65°). Freely sol in water. Aq soln (orange) is neutral. Slightly sol in alcohol. (Free base is sol in the usual organic solvents.)

THERAP CAT: Antischistosomal.

5406. Lucensomycin. FI 1163; Etruscomicina; Etruscomycin; Antibiotic FI 1163. $C_{36}H_{53}NO_{13}$; mol wt 707.83. C 61.09%, H 7.55%, N 1.98%, O 29.39%. Polyene antifungal antibiotic isolated from cultures of *Streptomyces lucensis:* Arcamone *et al., Giorn. Microbiol.* **4,** 119 (1957); Arcamone, Perego, *Ann. Chim. (Rome)* **49,** 345 (1959); Marini, Pennella, *Proc. Symp. Antibiotics Prague* (May 1959) p 148; Arcamone *et al.,* U.S. pat. **3,170,837** (1965 to Farmitalia). Structure: Guadiano *et al., Tetrahedron Letters* **1966,** 3559, 3567; *Gazz. Chim. Ital.* **96,** 1470 (1966); *Chim. Ind. (Milan)* **48,** 1327 (1966). Revised structure: R. C. Pandey, K. L. Rinehart, *J. Antibiot.* **29,** 1035 (1976).

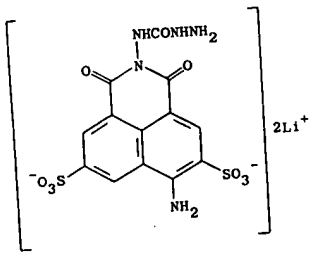


Crystalline powder. $[\alpha]_D^{20}$ +296° (pyridine), +50° (methanolic 0.1 *N* HCl). uv max: 218, 278, 290, 303, 318 nm ($E_{1cm}^{1\%}$ 300, 370, 780, 1170, 1098). Practically insol in water, anhydr alcohol, non-polar solvents; sol in pyridine, dimethylformamide. Unstable beyond pH 6-8, and to heat, light, or air. LD_{50} orally in mice: 1263 mg/kg.

THERAP CAT: Antifungal.

5407. Luciferin. A generic term referring to a substrate which, upon oxidation by the enzyme luciferase, produces bioluminescence. Luciferins isolated from different species may vary greatly in structure, although in many cases identical structures have been found in widely diverse animals. The most widely studied luciferins are those isolated from the sea pansey, *Renilla reniformis,* the ostracod, *Cypridina hilgendorfii,* the limpet, *Latia neritoides,* and the firefly, *Photinus pyralis (see* separate entry, Firefly Luciferin). Structure of *Renilla reniformis* luciferin: K. Hori *et al., Proc. Nat. Acad. Sci. USA* **74,** 4285 (1977). *Review:* M. J. Cormier *et al., Fortschr. Chem. Org. Naturst.* **30,** 1-60 (1973).

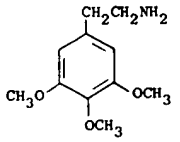
5408. Lucifer Yellow CH. *6-Amino-2-[(hydrazinocarbonyl)amino]-2,3-dihydro-1,3-dioxo-1H-benz[de]isoquinoline-5,8-disulfonic acid dilithium salt.* $C_{13}H_9Li_2N_5O_9S_2$; mol wt 457.25. C 34.15%, H 1.98%, Li 3.04%, N 15.32%, O 31.49%, S 14.02%. Highly fluorescent dye that reveals functional connection between cells by its movement from cell to cell, termed "dye-coupling": W. W. Stewart, *Cell* **14,** 741 (1978). Prepn: *idem, J. Am. Chem. Soc.* **103,** 7615 (1981). As tracer for electron microscopy: A. R. Maranto, *Science* **217,** 953 (1982). Selective uptake by retinal cells: P. V. Sarthy *et al., J. Comp. Neurol.* **206,** 371 (1982). *Review:* W. W. Stewart, *Nature* **292,** 17-21 (1981).



Fluffy orange hygroscopic powder. Absorption max (water): 280, 428 nm (ε 24200, 11900). Sol in water.

USE: As intracellular marker in biological systems.

(1919); Slotta, Heller, *Ber.* **63**, 3029 (1930); Späth, Becke, *Monatsh.* **66**, 327 (1935); M. U. Tsao, *J. Am. Chem. Soc.* **73**, 5495 (1951); K. Banholzer *et al., Helv. Chim. Acta* **35**, 1577 (1952). Novel synthesis: M. N. Aboulenein, A. I. Eid, *Acta Pharm. Suec.* **16**, 267 (1979). *Reviews:* Patel, *Progress in Drug Research* **vol. 11**, E. Jucker, Ed. (Birkhaüser Verlag, Basel, 1968) pp 11-47; Kapadia, Fayez, *J. Pharm. Sci.* **59**, 1699-1727 (1970).



Crystals, mp 35-36°. bp_{12} 180°. Moderately sol in water; sol in alcohol, chloroform, benzene; almost insol in ether, petr ether. Takes up CO_2 from the air and forms a cryst carbonate. LD_{50} i.p. in rats: 370 mg/kg, L. B. Speck, *J. Pharmacol. Exp. Ther.* **119**, 78 (1957).

Hydrochloride, $C_{11}H_{17}NO_3.HCl$, needles, mp 181°, sol in water, alcohol. LD_{50} i.p. in mice, rats, guinea pigs: 212, 132, 328 mg/kg, Hardman *et al., Toxicol. Appl. Pharmacol.* **25**, 299 (1973).

Sulfate dihydrate, $(C_{11}H_{17}NO_3)_2.H_2SO_4.2H_2O$, prisms, mp 183-186°, sol in hot water, methanol; sparingly sol in cold water and in ethanol.

Acid sulfate, $C_{11}H_{17}NO_3.H_2SO_4$, crystals, mp 158°.

Aurichloride monohydrate, $C_{11}H_{17}NO_3.HCl.AuCl_3.H_2O$, orange needles from water, mp 140-141° (dec). Very sol in alcohol and hot water.

Platinichloride, $(C_{11}H_{17}NO_3)_2.2HCl_4PtCl$, yellow needles from water, mp 187-188° (dec).

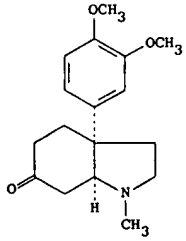
N-Benzoylmescaline, needles from aq alc, mp 121°. Very sol in alcohol and ether.

N-Methylmescaline, bp 130-140° (picrate mp 178°) and *N*-acetylmescaline, mp 94°, occur naturally.

Caution: May produce serious psychologic disturbances.

THERAP CAT: Exptl psychotomimetic.

5751. Mesembrine. *3a-(3,4-Dimethoxyphenyl)octahydro-1-methyl-6H-indol-6-one;* 3a-(3,4-dimethoxyphenyl)tetrahydro-1-methyl-6(3a*H*)-indolinone. $C_{17}H_{23}NO_3$; mol wt 289.36. C 70.56%, H 8.01%, N 4.84%, O 16.59%. Alkaloid used in preparing *Channa,* a drug of Southwest Africa. Occurs naturally as the (−)-form. From *Sceletium expansum* L., *S. tortuosum* L., *L. bolus* (formerly called *Mesembryanthemum expansum* L., *M. tortuosum* L.) *Ficodaceae* or *Aizoaceae:* Hartwick, Zwicky, *Apoth. Ztg.* **29**, 925 (1914); Rimington *et al., J. Vet. Sci. Animal Ind.* **9**, 187 (1938), *C.A.* **32**, 4279[9] (1938). Structure: Popelak *et al., Naturwiss.* **47**, 156 (1960). Configuration: P. W. Jeffs *et al., J. Am. Chem. Soc.* **91**, 3831 (1969). Synthesis of (±) form: Shamma, Rodriguez, *Tetrahedron Letters* **1965**, 4847; O. Hoshino *et al., Heterocycl.* **10**, 61 (1978); of (±)-form and *trans* isomer: Oh-Ishi, Kugita, *Chem. Pharm. Bull.* **18**, 299 (1970). Synthesis of (+)-form: Yamada, Otani, *Tetrahedron Letters* **1971**, 1133; *eidem, Chem. Pharm. Bull.* **21**, 2130 (1973). Stereoselective synthesis of (±)-form: Wijnberg, Speckamp, *Tetrahedron Letters* **1975**, 3963; *eidem, Tetrahedron* **34**, 2579 (1978); S. F. Martin *et al., J. Org. Chem.* **44**, 3391 (1979); S. Takano *et al., Chem Letters* **1981**, 1385. Enantioselective synthesis of natural mesembrine: *eidem, Tetrahedron Letters* **22**, 4479 (1981). Biosynthesis: Jeffs *et al., J. Am. Chem. Soc.* **93**, 3752 (1971); *eidem. Chem. Commun.* **1977**, 60. Review of mesembrine alkaloids: A. Popelak, G. Lettenbauer in *The Alkaloids,* R. H. F. Manske, Ed., **vol. IX** (Academic Press, New York, 1967) pp 467-481; R. V. Stevens in *The Total Synthesis of Natural Products* **vol. 3**, J. ApSimon, Ed. (Wiley, New York, 1977) pp 443-453.



(-)-mesembrine

Pale yellow oil. $bp_{0.3}$ 186-190°. $[\alpha]_D^{20}$ −55.4° (CH_3OH). Freely sol in alcohol, chloroform, acetone; slightly sol in ether. Practically insol in benzene, petr ether, alkalies.

Hydrochloride, $C_{17}H_{23}NO_3.HCl$, mp 205-206°. $[\alpha]_D^{20}$ −8.4° (CH_3OH).

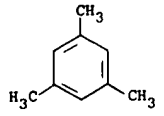
(+)-Form. (Partially optically active). Pale yellow oil. $[\alpha]_D^{20}$ +16.1° (c = 1.32 in CH_3OH).

(+)-Form hydrochloride, $C_{17}H_{23}NO_3.HCl$, crystals from 2-propanol, mp 206.5-207.5°. $[\alpha]_D^{20}$ +7.3° (c = 0.465 in CH_3OH).

(±)-Form. Colorless oil. $bp_{0.07}$ 178°.

(±)-Form hydrochloride, $C_{17}H_{23}NO_3.HCl$, mp 179-181°.

5752. Mesitylene. *1,3,5-Trimethylbenzene; sym*-trimethylbenzene. C_9H_{12}; mol wt 120.19. C 89.93%, H 10.06%. Occurs in coal tar and in petroleum crudes; prepd by dehydrating acetone with H_2SO_4: Adams, Hufferd, *Org. Syn.* **2**, 41 (1922).



Liquid; peculiar odor. d_4^{20} 0.8637. mp −44.8°. bp_{760} 164.7°; bp_{100} 98.9°; bp_{20} 61°; bp_{10} 47.4°; $bp_{1.0}$ 9.6°. n_D^{18} 1.49541. Practically insol in water (100 g H_2O dissolve 0.002 g). Miscible with alcohol, ether, benzene.

5753. Mesityl Oxide. *4-Methyl-3-penten-2-one;* isopropylideneacetone. $C_6H_{10}O$; mol wt 98.14. C 73.43%, H 10.27%, O 16.30%. $(CH_3)_2C{=}CHCOCH_3$. Made by distilling diacetone alcohol with a small amount of iodine: Conant, Tuttle, *Org. Syn.* **1**, 53 (1921). Condensation of acetone to mesityl oxide using sulfonated polystyrene-divinylbenzene resin as ion exchange catalyst: Klein, Banchero, *Ind. Eng. Chem.* **48**, 1278 (1956). Believed to be a mixture of two isomers.

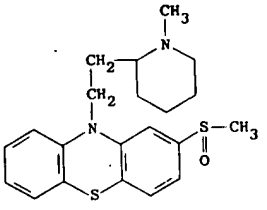
Colorless, oily liq; honey-like odor. d_4^{15} 0.8592. bp_{760} 130°; bp_{100} 72.1°; bp_{20} 26°; $bp_{1.0}$ −8.7°. Solidifies at −41.5° (also reported as −59°). Can be made to crystallize at low temp in petr ether. n_D^{22} 1.4425. Absorption spectrum: Morton, *J. Chem. Soc.* **1926**, 719. Sol in about 30 parts water; miscible with most organic liqs. Flash pt: 87°F (30.6°C). Lethal concn for rats in air: 2500 ppm, *Handbook of Toxicology* **vol. 1**, W. S. Spector, Ed. (Saunders, Philadelphia, 1956) pp 342-343.

USE: Solvent for nitrocellulose, many gums and resins, particularly vinyl resins. In lacquers, varnishes and enamels. In making methyl isobutyl ketone.

5754. Mesna. *2-Mercaptoethanesulfonic acid sodium salt;* sodium mercaptoethanesulfonate; UCB 3983; Mistabron; Mistabronco; Mucofluid; Uromitexan. $C_2H_5NaO_3S_2$; mol wt 164.17. C 14.63%, H 3.07%, Na 14.00%, O 29.24%, S 39.06%. $[HSCH_2CH_2SO_3]^-Na^+$. Prepn: Lipovich, *J. Appl. Chem. USSR* **18**, 718 (1945); Schramm *et al., J. Am. Chem. Soc.* **77**, 6231 (1955); Reppe *et al., Ann.* **601**, 111 (1956). Synthesis and properties: Petrun'kin, *C.A.* **51**, 5693a (1957) and **54**, 24379c (1960). Prepn of salts: Neth. pat. **Appl. 6,605,816** corresp to Morren, U.S. pat. **3,567,835** (1966 and 1971, both to U.C.B.).

THERAP CAT: Mucolytic.

5755. Mesoridazine. *10-[2-(1-Methyl-2-piperidinyl)ethyl]-2-(methylsulfinyl)-10H-phenothiazine;* TPS-23. $C_{21}H_{26}N_2OS_2$; mol wt 386.59. C 65.24%, H 6.78%, N 7.25%, O 4.14%, S 16.59%. Prepn: Renz *et al.,* U.S. pat. **3,084,161** (1963 to Sandoz). Pharmacology and toxicology: Loew *et al., Boll. Chim. Farm.* **106**, 332-371 (1967).



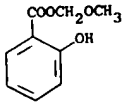
Oily product.

Benzenesulfonate, *mesoridazine besylate, NC-123, Lidanar, Lidanil, Serentil.* LD_{50} in mice: 33 mg/kg i.v.; 611 mg/kg s.c.; 346 mg/kg orally, Maruyama *et al., C.A.* **68,** 76856h (1968).

Tartrate, $C_{21}H_{26}N_2OS_2.C_4H_6O_6$, crystals from ethyl acetate, mp 115-120°.

THERAP CAT: Antipsychotic.

5756. Mesotan. *2-Hydroxybenzoic acid methoxymethyl ester;* methoxymethyl salicylate; Ericin; Salmester. $C_9H_{10}O_4$; mol wt 182.17. C 59.33%, H 5.53%, O 35.13%.



Yellowish, clear, faintly aromatic, oily liquid. d^{15} 1.2. bp_{42} 162°. Slightly sol in water; miscible with alcohol, benzene, chloroform, ether, fixed oils. *Keep dry and well closed.*

5757. Mesoxalic Acid. *Oxopropanedioic acid;* ketomalonic acid; oxomalonic acid. $C_3H_2O_5$; mol wt 118.05. C 30.52%, H 1.71%, O 67.77%. HOOCCOCOOH. Occurs in *Medicago sativa* L., *Leguminosae;* has been found in beet molasses. Prepd by boiling a soln of alloxan and lead acetate: Deichsel, *J. Prakt. Chem.* [1] **93,** 194 (1864). By electrolysis of *d*-tartaric acid in alkaline soln: *Chem. Zentr.* **1922, III,** 871. Laboratory prepn from dibromomalonic acid: Conrad, Reinbach, *Ber.* **35,** 1819 (1902); from malonic ester and N_2O_3: Curtiss, *Am. Chem. J.* **35,** 477 (1906)

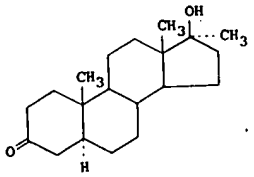
Monohydrate, $C_3H_2O_5.H_2O$, *dihydroxymalonic acid.* Begins to melt at 113-114° and is clear at 121°. Very sol in water; sol in alc, ether.

Diethyl ester, $C_7H_{10}O_5$, *ethyl oxomalonate.* Liquid. bp_{19} 105-107°. $d_4^{15.6}$ 1.1419. $n_D^{15.6}$ 1.419. Prepn: A. W. Dox, *Org. Syn.* **coll. vol. I,** 266 (2nd ed., 1941). Diethyl ester of dihydroxymalonic acid ($C_7H_{12}O_6$) is obtained from the crude ester mixture by fractional distn. Crystals, mp 57°. Sol in water, alcohol.

5758. Mesquite Gum. Sonora; Prosopis gum. Gathered from small thorny trees abundant in the arid regions of the Western United States and as far south as Chile: *Prosopis juliflora* (Swartz) DC., *P. dulcis* Kunth., *P. horrida* Kunth., *P. inermis* H.B.K., *P. glandulosa* Torr., *P. pubescens* Benth., *P. spicigera* L., and other species of *Prosopis, Leguminosae.* Mesquite gum resembles acacia (gum arabic) in its physical and chemical characteristics. Review of structure work: F. Smith, R. Montgomery, *The Chemistry of Plant Gums and Mucilages* (Reinhold, New York, 1959) pp 175, 288-291.

USE: Substitute for acacia. Potential source of L-arabinose and D-glucuronic acid, *cf.* C. L. Mantell, *The Water-Soluble Gums* (Reinhold, New York, 1947) pp 72-73.

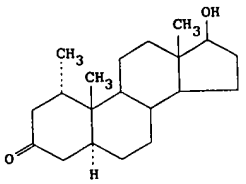
5759. Mestanolone. *17β-Hydroxy-17-methyl-5α-androstan-3-one;* 17β-hydroxy-17α-methyl-3-androstanone; 17α-methylandrostan-17β-ol-3-one; 17α-methylandrostan-3-on-17β-ol; Androstalone. $C_{20}H_{32}O_2$; mol wt 304.46. C 78.89%, H 10.59%, O 10.51%. Prepd by the oxidation of 17-methyl-3,17-androstanediol: Ruzicka *et al., Helv. Chim. Acta* **18,** 1487 (1935); Swiss. pat. **208,080** (1940 to Ciba).



Crystals from ethyl acetate, mp 192-193°. Insol in water. Sol in acetone, alcohol, ether, ethyl acetate.

THERAP CAT: Androgen.

5760. Mesterolone. *17-Hydroxy-1-methylandrostan-3-one;* 1α-methyl-5α-androstan-17β-ol-3-one; 1α-methyl-5α-dihydrotestosterone; Androviron; Proviron; Mestoranum. $C_{20}H_{32}O_2$; mol wt 304.46. C 78.89%, H 10.59%, O 10.51%. Prepn of acetate: R. Wiechert, Ger. pat. **1,122,944** corresp to U.S. pat. **3,361,773** (1962, 1968 to Schering, AG).

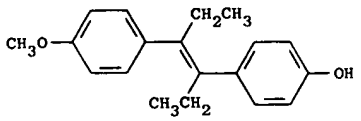


Crystals from ethyl acetate, mp 203.5-205.0°. $[\alpha]_D^{20}$ +17.6° (c = 0.875 in $CHCl_3$).

Acetate, $C_{22}H_{34}O_3$, *17β-acetoxy-1α-methyl-5α-androstan-3-one.* Crystals, mp 169-170°. $[\alpha]_D^{25}$ +16.5° (c = 0.88 in $CHCl_3$).

THERAP CAT: Androgen.

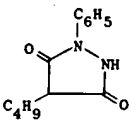
5761. Mestilbol. *4-[1-Ethyl-2-(4-methoxyphenyl)-1-butenyl]phenol; α,α'-diethyl-4'-methoxy-4-stilbenol;* diethylstilbestrol monomethyl ether; 3-*p*-hydroxyphenyl-4-*p*-methoxyphenyl-3-hexene; monomestrol. $C_{19}H_{22}O_2$; mol wt 282.37. C 80.81%, H 7.85%, O 11.33%. Prepn: Reid, Wilson, *J. Am. Chem. Soc.* **64,** 1625 (1942); U.S. pat. **2,385,468** (1945). The monoether is sepd from the diether by its greater soly in 0.4*N* alcoholic KOH. Other syntheses: Ger. pat. **708,202** (1941); Wiles, Biggerstaff, *J. Am. Chem. Soc.* **67,** 789 (1945). *See also* Dimestrol.



Needles from benzene + petr ether, mp 116-117.5°; leaflets from 70% alc, mp 114°; v. Pallos, *Arch. Gynäkol.* **170,** 355, 385 (1940), reports mp 120-121°. Distills at 185-195° at 0.3 mm Hg. Is generally more sol than the dimethyl ether of diethylstilbestrol. Practically insol in water. Sol in alcohol, dil aq or alcoholic solns of alkali hydroxides, and in vegetable oils; freely sol in acetone, ether.

5762. Mestranol. *3-Methoxy-19-norpregna-1,3,5(10)-trien-20-yn-17-ol;* 17α-ethynyl-3-methoxy-1,3,5(10)-estratrien-17β-ol; 17α-ethynylestradiol 3-methyl ether; Norquen; Ovastol. $C_{21}H_{26}O_2$; mol wt 310.42. C 81.25%, H 8.44%, O 10.31%. Prepn: Colton, U.S. pat. **2,666,769** (1954 to Searle); *J. Am. Chem. Soc.* **79,** 1123 (1957). Comprehensive description: H. A. El-Obeid, A. A. Al-Badr, in *Analytical Profiles of Drug Substances* **vol. 11,** K. Florey, Ed. (Academic Press, New York, 1982) pp 375-406.

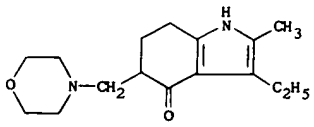
yl-3,5-dihydroxy-4-butylpyrazolidine; monophenylbutazone; Arcomonol Tablets; Mobutazon; Mobuzon; Monazan; Monobutyl; Monorheumetten; Reumatox. $C_{13}H_{16}N_2O_2$; mol wt 232.27. C 67.22%, H 6.94%, N 12.06%, O 13.78%. Preparation: Büchi *et al., Helv. Chim. Acta* **36**, 75 (1953); **Brit. pat. 839,057** (1960 to Comm. Farm. Milanese).



Crystals from ethanol + water, mp 102-103°. uv max (ethanol): 240, 275 nm ($E^{1\%}_{1cm}$ 443, 245). LD_{50} i.v. in mice: 600 mg/kg, Schoetensack, *Arch. Exp. Pathol. Pharmakol.* **233**, 365 (1958).

THERAP CAT: Anti-inflammatory.

6086. Molindone. *3-Ethyl-1,5,6,7-tetrahydro-2-methyl-5-(4-morpholinylmethyl)-4H-indol-4-one;* 3-ethyl-6,7-dihydro-2-methyl-5-(morpholinomethyl)indol-4(5*H*)-one. $C_{16}H_{24}N_2O_2$; mol wt 276.37. C 69.53%, H 8.75%, N 10.14%, O 11.58%. Prepn: **Belg. pat. 670,798** (1966 to Endo), *C.A.* **65**, 7148f (1966). Pharmacology: Sugerman, Herrmann, *Clin. Pharmacol. Ther.* **8**, 261 (1967); Claghorn, *Curr. Ther. Res.* **11**, 524 (1969); Guerrero-Figueroa *et al., ibid.* **15**, 508 (1973).

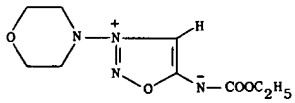


Crystals, mp 180-181°.

Hydrochloride, *EN 1733 A, Lidone, Moban.* LD_{50} orally in rats: 261 mg/kg, E. I. Goldenthal, *Toxicol. Appl. Pharmacol.* **18**, 185 (1971).

THERAP CAT: Antipsychotic.

6087. Molsidomine. *N-(Ethoxycarbonyl)-3-(4-morpholinyl)sydnone imine; N*-carboxy-3-morpholinosydnonimine ethyl ester; morsydomine; SIN-10; Corvaton; Molsidolat; Morial; Motazomin. $C_9H_{14}N_4O_4$; mol wt 242.23. C 44.62%, H 5.83%, N 23.13%, O 26.42%. A member of a class of non-benzene aromatic, heterocyclic and mesoionic type of compounds previously unknown in the pharmaceutical industry. Developmental work on sydnone imines: Brookes, Walker, *J. Chem. Soc.* **1957**, 4409. Prepn: Masuda *et al.*, **Japan. pat. 6,265('70)** (to Takeda), *C.A.* **73**, 25485g (1970) and *Chem. Pharm. Bull.* **19**, 72 (1971). Stability studies: Asahi *et al., ibid.* **19**, 1079 (1971). Pharmacological studies: Kikuchi *et al., Japan. J. Pharmacol.* **20**, 102, 187, 253 (1970); Hashimoto *et al., Arzneimittel-Forsch.* **21**, 1329 (1971). Metabolism: S. Tanayama *et al., Xenobiotica* **4**, 175 (1974). *Review: Japan. Med. Gaz.* **8**(9), 10 (1971).



Colorless crystals or white cryst powder, practically tasteless and odorless, mp 140-141° (toluene). Freely sol in $CHCl_3$. Sol in dil HCl, ethanol, ethyl acetate, methanol; sparingly sol in water, acetone, benzene. Very slightly sol in ether, petr ether. pK 3.0 ± 0.1 at 100°. Most stable in aq solns pH 5-7; least stable in very alkaline solns. uv max ($CHCl_3$): 326 nm. Sensitive to light of $\lambda < 320$ mμ. LD_{50} mouse, rat (g/kg): ≃0.76, 1.36 s.c.; ≃0.83, 0.80 i.v.; ≃0.73, 1.25 i.p.; ≃0.83, 1.13 orally.

THERAP CAT: Coronary vasodilator; antihypertensive.

6088. Molybdenum. Mo; at. wt 95.94; at. no. 42; valences 2,3,4,5,6. Naturally occurring isotopes: 98 (23.75%); 96 (16.5%); 95 (15.7%); 92 (15.86%); 94 (9.12%); 100 (9.62%); 97 (9.45%); artificial radioactive isotopes: 88-91; 93; 99; 101-105. Its most important ores are molybdenite, MoS_2, and wulfenite, $PbMoO_4$. Occurrence in the earth's crust: 1-1.5 ppm. Discovered in 1778 by Scheele; isolated in 1782 by Hjelm. Methods of preparation: L. Northcott, *Molybdenum* (Academic Press, New York, 1956) 222 pp; Hein, Herzog, in *Handbook of Preparative Inorganic Chemistry* **vol. 2**, G. Brauer, Ed. (Academic Press, New York, 2nd ed., 1965) pp 1401-1402. Important trace element; participates in biochemical redox reactions such as N_2-fixation: Spence, *Coord. Chem. Rev.* **4**, 475 (1969). Review of molybdenum and its compds: Rollinson, "Chromium, Molybdenum and Tungsten" in *Comprehensive Inorganic Chemistry* **vol. 3**, J. C. Bailar Jr. *et al.*, Eds. (Pergamon Press, Oxford, 1973) pp 622-623, 700-742; R. Q. Barr in Kirk-Othmer *Encyclopedia of Chemical Technology* **vol. 15** (Wiley-Interscience, New York, 3rd ed., 1981) pp 670-682. Biochemical review: *Bioinorganic Chemistry* **II**, K. N. Raymond, Ed. (A.C.S., Washington, 1977) pp 353-430.

Dark-gray or black powder with metallic luster or coherent mass of silver-white color; body-centered cubic structure. mp 2622°: Worthing, *Phys. Rev.* [2] **25**, 846 (1925); bp about 4825°. d 10.28. Spec heat 5.68 cal/g-atom/deg; heat of fusion: 6.6 kcal/g-atom; heat of vaporization: 142 kcal/-g-atom: D. R. Stoll, G. C. Sinke, *Thermodynamic Properties of the Elements*, Advances in Chemistry Series **18**, (American Chemical Society, Washington, 1956) pp 23, 130-131. Fairly stable at ordinary temp; oxidized to the trioxide at a red heat; slowly oxidized by steam. Not attacked by water, by dil acids or by concd hydrochloric acid. Practically insol in alkali hydroxides or fused alkalies. Reacts with nitric acid, hot concd sulfuric acid, fused potassium chlorate or nitrate. Attacked by fluorine at ordinary temp, by chlorine or bromine at a red heat.

Human Toxicity: Limited data suggest low order of toxicity. *See* E. Browning, *Toxicity of Industrial Metals* (Appleton-Century-Crofts, New York, 1969) pp 243-248.

USE: In the form of ferromolybdenum for manufg special steels for tools, boiler plate, rifle barrels, propeller shafts; electrical contacts, spark plugs, x-ray tubes, filaments, screens and grids for radio tubes; in the production of tungsten; glass-to-metal seals; nonferrous alloys; in colloidal form as lubricant additive.

6089. Molybdenum Disulfide. MoS_2; mol wt 160.08. Mo 59.94%, S 40.06%. Occurs as the mineral *molybdenite*, which is the principal source of molybdenum. Lab prepn: Bell, Herfert, *J. Am. Chem. Soc.* **79**, 3351 (1957).

Lead-gray, lustrous powder; the artificially prepd sulfide is black and lustrous. d^{15}_{15} 5.06; mp 2375°. Begins to sublime at 450°. Insol in water or dil acids.

USE: Dry lubricant and lubricant additive. Hydrogenation catalyst.

6090. Molybdenum Hexafluoride. F_6Mo; mol wt 209.95. F 54.30%, Mo 45.70%. MoF_6. Prepd by direct fluorination of powdered molybdenum: Ruff, Ascher, *Z. Anorg. Allgem. Chem.* **196**, 418 (1931); from MoO_3 and SF_4: Oppengard *et al., J. Am. Chem. Soc.* **82**, 3825 (1960).

Volatile, white, cubic crystals. Very hygroscopic. d^{19}_{14} 2.543. mp 17.5°. bp 35.0°. Hydrolyzed by water. Forms blue-white clouds in moist air. Soly in anhydr HF: 1.5 moles/1000 g HF, Frlec, Hyman, *Inorg. Chem.* **6**, 1596 (1967). Should be stored in quartz ampuls.

6091. Molybdenum Sesquioxide. Mo_2O_3; mol wt 239.90. Mo 79.99%, O 20.01%.

Grayish-black powder. Very slightly sol in acids.

Combination with ferrous sulfate *Mol-Iron (obsolete).*

THERAP CAT: Hematinic (combination with ferrous sulfate).

6092. Molybdenum Trioxide. Molybdic anhydride. MoO_3; mol wt 143.95. Mo 66.66%, O 33.34%. Prepn from ammonium molybdate: Schumb, Hartford, *J. Am. Chem. Soc.* **56**, 2613 (1934).

White or slightly yellow to slightly bluish powder or granules. d^{26}_4 4.696. Melts at 795° to dark-yellow liquid which solidifies to a yellowish-white cryst mass; sublimes at higher temp; bp 1155°. Sol in water (28°) 0.490 g/liter. Sol in concd mineral acids, in solns of alkali hydroxides, ammonia or potassium bitartrate; after strong ignition it is very slight-